HORMONES IN INVERTEBRATES

BY

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PREFACE

'ENDOCRINOLOGISTS are just now in a bigger hurry than any other group of investigators in the world', writes Riddle (1935), and that is why I have found it, if not necessary, at least useful to try to make a more complete summary of what is known at present about hormonal reactions in invertebrates than that found in my paper of 1937. I hope that this subject will be of interest not only to those who, like myself, are working with invertebrates but also—on account of the general laws which control the whole animal kingdom, including Man—to vertebrate physiologists and endocrinologists of the medical profession. In my treatment of this subject I have included a fairly complete account of the anatomy and histology of the few incretory organs as yet detected in invertebrates, since I am firmly convinced of the necessity for co-operation between anatomists and physiologists in investigating this most fascinating field of biological science.

The first comprehensive paper upon the hormonal reactions of invertebrates was published in German by G. Koller (1929). Later there appeared two papers in Italian by B. de Lerma (1934, 1936), and in 1937 and 1938 not less than three more extensive treatises in German on the same subject: in July 1937 my *Inkretorische Organe und Hormonfunktionen bei den Wirbellosen*, in November 1937 G. Koller's *Hormone bei wirbellosen Tieren*, and in January 1938 Th. von der Wense's *Wirkungen und Vorkommen von Hormonen bei wirbellosen Tieren*. I owe to Koller's work of 1937, as also to his paper of 1929, several ideas, especially in the chapters on metamorphosis in insects and colour change in Crustaceans; and from the book by von der Wense I have obtained much information about the pharmacodynamic investigations into the action of vertebrate hormones on invertebrates.

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INTRODUCTION

AS recently as 1933 Pugliese held the view that no undoubted incretory activity in invertebrates nor any certain influence of vertebrate hormones on invertebrates had up to that time been found. He was therefore of the opinion that the invertebrates receive their hormones with vegetable food. This book proves, however, that several incretory organs, and still more numerous physiological processes which cannot be explained without the theory of a hormonal function, are already known in invertebrates. But it is of course true that our knowledge on this subject is very imperfect and that it has only just begun to become a branch of natural science that can be comprehensively treated with profitable result.

The old definition of a hormone as a substance which is secreted into the blood by a ductless gland and exerts a specific physiological effect at another place in the body (even if present in very small quantities) is no longer satisfactory. Especially in invertebrates, in which there is no relation between the many known instances of physiological processes which must be classified as hormonal and the relatively few structures identified as true incretory organs analogous with those of vertebrates, the old definition cannot be used. Furthermore, there are many invertebrates which do not possess blood and in which the hormones, if they exist, must be transported by means of diffusion through the protoplasm. We also nowadays know several substances whose action must be said to be hormonal, but which are certainly not produced in incretory glands but in portions of organs whose chief function is quite other than hormonal. There are, further, the growth hormones, the wound hormones, the organizer problem in embryonic development, the localized chemo-differentiators (Huxley & de Beer, 1934), the 'gene hormones' (intracellular hormones of Goldschmidt), whose real existence and transportability through the blood have been experimentally proved in investigations of extreme general interest of recent years. Finally, there is the problem of drawing a distinction between hormones and vitamins—in some instances no easy matter (Randoin & Simonnet, 1928). These facts and problems have in combination led to the production

of several comprehensive theoretical papers in which a new hormone concept is discussed or put forward—e.g., Goldschmidt (1931), Bethe (1932), Huxley (1935), Kisch (1936), and Koller (1937).

On practical and also on theoretical grounds the hormone concept of Koller (1937) is accepted in this work; the hormones are considered as organic substances which are produced by the organism for its own use and have a specific regulatory function within it. As far as we know now the hormones are further characterized by the following qualities. They are active, even when present in very small amounts; they are transported humorally; their activity is not limited to the species or the genus, and they mostly withstand boiling without destruction.

Koller (1937) also gives a very attractive classification of hormones, founded on the kind of secretion and the nature and situation of the source within the body where the hormones are produced and where they act. Thus the hormones are named (1) cell hormones ('Zellhormone'), (2) non-glandular tissue hormones ('aglanduläre Gewebshormone'), and (3) glandular tissue hormones ('glanduläre Gewebshormone' or 'Drüsenhormone'). The cell hormones, which include practically the same substances as Huxley's (1935) 'diffusion hormones', comprise the gene hormones and hormones in Protozoa. The non-glandular tissue hormones comprise the heart-stimulating hormones, the neuro-secretory hormones, and a special contractive substance in the worm *Physcosoma*. Finally the glandular tissue hormones include the sex hormones, hormones regulating metamorphosis in Insects, and the colour-change hormones, all of which (with very few exceptions) are—or in all probability are—produced in endocrine glands. Koller lays stress upon the difficulty of drawing a strict distinction between the non-glandular and the glandular tissue hormones. I believe that the distinction between these two last-named groups of hormones is not only difficult but at present quite impossible to draw. It seems, for instance, as if metamorphosis in Insects is in part regulated by hormones produced by certain rather well-defined incretory organs, but in part by the brain itself, i.e. by a neuro-secretory organ. Thus, although I consider the classification of hormones by Koller very logical and in the main suitable for a future definitive treatment of these problems, I prefer for

the present to use a mainly practical classification which will be understood by a glance at the list of contents.

As to the cell hormones of the Protozoa (which include adrenaline and acetylcholine), and the many instances of an action of vertebrate hormones on invertebrates and vice versa dealt with in the first two chapters, I must of course point out that we do not yet know if these substances, which are found within the body of invertebrates or which act upon them, also really function as normal hormones in primitive animals. It may be, as Pflugfelder (1937) has suggested, that the hormones of invertebrates do not have the same specific action as those of the highest animal groups, and it is also possible that new hormones have been developed during the evolution of the animal kingdom. But I think that we have already collected enough evidence about hormones in invertebrates (for instance, about the occurrence of adrenaline in these animals and the action of the same hormone upon different invertebrate groups; cf. pp. 13, 22 and 142) to be able to predict that in the future it will be possible in a much higher degree than at present to exchange hormones between the chief divisions of animals. I believe also that it is no over-fanciful speculation to think that some invertebrate hormones, which are still only slightly known through their physiological actions, may one day be used for important experimental and perhaps pharmacological purposes in vertebrates, including man.

THE INFLUENCE OF VERTEBRATE HORMONES ON INVERTEBRATES

1. The Thyroid Gland

A. Protozoa. There have been several investigations on the possibility of affecting the rate of fission and other vital processes in Protozoa with dried thyroid gland, with extracts of the same gland, or with thyroxine, but these researches have not given consistent results. With various (unpurified) preparations of the thyroid gland Nowikoff (1908), Shumway (1914–29), Budington & Harway (1915), and Abderhalden & Schiffman (1922) observed a more or less marked acceleration of the rate of fission in Protozoa which was referred to a specific action of the thyroid hormone. The correctness of this interpretation was, however, denied by Ball (1925) and Lwoff (1925), who believed that the supply of the thyroid preparations to the water in which the Protozoa (commonly *Paramecium*) were living had produced more favourable nutritive conditions, this explaining the more rapid rate of fission. In this connexion it is also noteworthy that several investigations into the influence of pure thyroxine on the rate of fission of the *Paramecia* have yielded negative results; sometimes a lower rate of fission was observed. Thus Cori (1923) observed a stimulation of reproduction with thyroid extracts but a much feebler action with thyroxine; and Breindl (1931) in general did not observe any positive influence on the rate of fission in several species of Ciliata Infusoria, belonging to the genera *Paramecium*, *Stylonychia*, and *Spirostomum*. Woodruff & Swingle (1924), Torrey, Riddle, & Brodie (1925), and Rhodenburg (1930) also noticed a more rapid rate of fission by using impure preparations of the thyroid gland, but a slower fission under the influence of pure thyroxine. Finally, Wertheimer (1928) and Capua (1931) did not note any positive action of thyroxine on the fission of Protozoa.

It is interesting that those authors who have noticed an increased rate of fission in Protozoa following an administration of thyroid preparations have also observed that the size of the animals simultaneously drops below the average. According to

Nowikoff (1908) this did not depend upon the higher rate of fission but upon a specific action of the thyroid extract. Torrey, Riddle, & Brodie (1925) have investigated the influence of thyroxine on the function of the contractile vacuoles, and found that this hormone promoted their pulsations and increased the number of the radiating canals, whereas Burge & Estes (1927) were not able to find any essential increase of the general metabolism in *Paramecium*.

The results which have been obtained in experiments with different preparations of the thyroid gland in Protozoa have thus been to a considerable degree contradictory. Kalmus (1931), Koller (1937), and von der Wense (1938) explain this on the basis of the different action of thyroxine solutions of different concentration, the different rate of fission in different cultures of Protozoa, and the immanent nutritive value of dried preparations of thyroid which may exercise a direct influence on the animals themselves and an indirect action upon the bacteria which constitute their most important food.

B. **Coelenterata.** The Coelenterata have still only been tested for their reactions to vertebrate hormones to an insignificant extent. Torrey (1934) has shown, however, that thyroxine solutions of a concentration of 1: 100,000 to 1: 1,400,000 checked the regeneration of hydranths in *Pennaria tiarella* when these had been cut off the stem of the colony. After a shorter treatment with the thyroxine solutions the number of regenerated hydranths was found to increase compared with the controls, but according to Torrey this could not with certainty be referred to a specific action of the hormone.

C. **Vermes.** There have been very few investigations into the action of thyroid preparations in worms; but one study, by Schmidt (1935), is of special interest. Schmidt investigated the fresh-water Polychaete worm *Lycastis ranauensis* which has been introduced into Germany from the East Indies and cultivated with considerable success; it has also been tested for its susceptibility to other vertebrate hormones (Feuerborn, 1936). According to Schmidt a treatment of young *Lycastis* with thyroid gland preparations promoted precocious sexual maturity, including a more rapid development of ripened eggs. In this connexion it is of interest that different commercial preparations yielded a different result, some of them stimulating the

development of the ova themselves, others the growth of the nutritive cells of the ovaries. Iodine which was not bound to organic molecules gave only negative results. The second generation of animals which had been treated with thyroid also showed a subsequent effect—they matured sexually earlier than animals which had not been treated. The thyroid preparations further stimulated the metabolism and improved the general physiological condition, the amount of blood-pigment increased, and an illness described by Feuerborn as lycastinosis (during which the blood-pigment is reduced) was cured by treatment with thyroid preparations. On the other hand, these have no influence upon growth and the regeneration processes.

D. Echinodermata. Most of the investigations into the action of thyroid preparations upon Echinoderms deal with their influence upon the rate of cleavage of the earlier embryological stages. Though Kollmann (1933) did not find any such influence in *Paracentrotus lividus*, Ludwig, Ries, & Ries (1935), observed that thyroxine prevented fertilization but strongly stimulated cell-division. Most of the authors, have, however, found a retarded development of ova under the influence of thyroxine: thus Butler (1928) in *Arbacia*, Torrey (1928) in *Echinometra*, Zavrél (1929) in *Paracentrotus*, and Runnström (1929) in *Antedon*. Ungar & Zerling (1933) observed no action of thyroxine upon the first cleavage stages in *Psammechinus miliaris*; whereas from the morula stage onwards strong solutions of thyroxine (1 : 50,000–1 : 800,000) have a retarding action, weak solutions (1 : 850,000–1 : 2,000,000) favour the development. Finally, Ashbel (1935) has found a stimulating influence of the thyroid preparation elyteran (Bayer) upon the oxygen consumption of Echinoderm ova, a result which could not be obtained with synthetic thyroxine.

E. Mollusca. The investigations thus far published on the action of thyroid preparations on Mollusca are contradictory. Thus in embryos of *Physa fontinalis*, Hykès (1930) sometimes observed a positive, sometimes a negative, influence on the development when he used thyroxine solutions in concentrations of 1 : 100,000 to 1 : 500,000. On the other hand, Susaeta (1930) noticed a faint acceleration of the first cleavage divisions in *Barnea candida* with weaker extracts of thyroid and a

retardation with more concentrated extracts. Chatzillo (1936), however, found accelerated development in 60 per cent. of investigated young *Limnaea stagnalis* under the influence of thyroid optones, though only during a certain period of the development.

Ashbel (1935) has examined the influence of elyteran on the oxygen consumption of mollusc ova and noticed the same increase as in Echinoderms. This agrees with the results obtained by Duskowa (1932), who observed an intensified oxygen consumption in *Limnaea stagnalis* after the addition of thyroid extracts to the aquarium water. This increase was not due to the addition of albuminous substances to the water.

F. **Arthropoda.** In Crustacea too there are discordant results concerning the influence of thyroid preparations on development. Thus Resnicenko (1927) did not observe any action of thyroid extracts on the development of *Cyclops strenuus*, and Banta & Brown (1929) noticed no effects of the addition of dried thyroid substance to the food in Cladocera. On the other hand, Vecchi (1920) says he obtained a positive result from the administration of dried thyroid substance to *Cyclops*, and Ciabetta & Floris (1930) noticed in *Artemia salina* (as in vertebrates) a more rapid rate of differentiation but a diminished body-size under the influence of thyroid extracts. These results were also said to be followed by an increased fertility and a lower mortality.

Of special interest is the investigation by Romeis (1925) on the action of thyroid upon the carbohydrate metabolism in *Astacus fluviatilis*. Romeis fed the crayfishes only on thyroid gland for five months, but this did not have any influence on the body-weight or on the amount of glycogen within the organs; nor did he observe any toxic action of the glandular material. Romeis's explanation is that the secretion of the hepatopancreas (the digestive gland) in *Astacus* is able to transform the hormone of the thyroid into inactive substances.

As for further investigations on this subject, it may be mentioned that Hykès (1926) noticed a stimulation of the heart-rhythm in *Daphnia magna* and *Daphnia pulex* under the influence of thyroidin; and that thyroxine according to Ashbel (1935) increases the oxygen consumption in the ova of Crustacea up to three times the normal amount. This agrees with the results of Davis & Hastings (1936), who also found increased oxygen

consumption in surviving segments of the heart of *Limulus polyphemus*, which increase is not due to increased activity of the heart as such, but probably to the action of thyroxine upon the cells of the heart-muscles.

In insects several investigations have yielded negative or practically negative results for the influence of thyroid preparations upon development and growth, but almost the same number of investigations have, on the other hand, given positive results. It is not, however, in all instances quite certain that these positive results are due to a specific action of the thyroid hormone. The former group of investigations includes the following papers.

Romeis & Dobkiewicz (1920) examined the influence of an administration of thyroid gland on the larvae of *Calliphora vomitoria*. At first the experimental larvae developed slower than the controls and moulted later, but during the later stages the advantage was counterbalanced and neither the pupae nor the imagines showed any difference from the normal animals. Kahn (1921), Cotronei (1923), and Remy (1923, 1924) fed larvae of different insects (*Corethra*, *Ecdyurus*, *Tenebrio*, *Lucilia*, *Sarcophaga*, *Plagioderma*, and *Bombyx* (that is, members of the orders Diptera, Lepidoptera, Coleoptera, and Ephemerida) with dried thyroid gland or other preparations of the same organ and obtained no positive results except for Kahn's observation that the colour and form of treated animals was affected. When Kopec (1926) fed larvae of *Lymantria dispar* and *Pieris brassicae* with thyroid tablets and Lugol's solution, he found indeed a slightly lower weight in the treated animals, but no influence upon the length of the larval development or the date of pupation. Nor did Resnicenko (1927) find any influence of thyroid extracts on the development in *Drosophila melanogaster* other than a prolongation of the larval stage following treatment with more concentrated solutions. By investigations which were continued over thirteen generations Dobkiewicz (1928) confirmed this statement for the same species; neither the fertility, reproduction, body-proportions, nor the time of development of the treated insects differed from the normal, and the feeding with thyroid preparations was not in any way injurious to the animals. Practically the same results were obtained by Dobkiewicz (1928), after feeding eight successive

generations of *Dermestes frischii* with thyroid. Negative results as regards development were also obtained by Hahn (1929) after feeding larvae of *Vanessa io* with thyroid preparations. Janda (1930) found no influence upon growth, metamorphosis, or specific characters in *Anthrenus muscorum* and *Dixippus morosus* during three years of experiment; neither did Bray (1933) in larvae of *Calliphora*. Finally, Fleischmann (1929) and Koller (1932) have tried the action of pure thyroxine in insects, the former on larvae of *Lymantria dispar* and *Celerio vespertilio*, the latter on *Drosophila*, without being able to determine any influence upon the development, the growth, the fertility, or the body-size. Fleischmann observed at the same time that the larvae of *Lymantria* and *Celerio* were remarkably insusceptible to the poisonous action of thyroxine. Thus a dose of 0·3 mg. which would kill a mouse had no influence upon the larva of *Celerio*. This is because the hormone within the body of these Lepidoptera is very soon transformed into a non-injurious substance, as Romeis (1925) found in *Astacus fluviatilis*.

Against these reported cases of negative results stand the following more or less obvious positive observations. Abderhalden (1919) tested the influence of hydrolysed thyroid substance on the larvae of *Deilephila euphorbiae*. The same substance has a positive action on tadpoles (diminishing their size), and from the larvae of *Deilephila* which were fed with thyroid Abderhalden bred some strikingly small but otherwise normal individuals, and some animals with abnormal pattern and imperfectly developed wings. Terao & Wakamori (1924, 1931), too, obtained unusually small larvae of *Bombyx mori* after feeding with thyroid substance, and the second generation, which had received normal food, gave rise to particularly small butterflies. In this instance it seems as if the activity of the hormone is not fully exhausted before the second generation. Magandda (1928) treated larvae of *Pieris brassicae* with thyroid extracts and observed a more rapid development after a shorter treatment, but a slower metamorphosis after a longer treatment; Kotsovsky (1934) remarks that thyroxine shortens the lifetime of the common house-fly during the autumn, and Brannon (1934) that the duration of the pupa stage in *Lucilia sericata* diminishes under the influence of thyroid preparations. Finally, Alpatov (1929) found a more rapid development and therefore an increased

body-size in larvae of *Drosophila* after thyroid feeding, and Zavrél (1927, 1930, 1931) observed in the same circumstances a considerably increased growth in larvae of Chironomidae (*Tanytarsus*, *Chironomus*). As feeding with thymus gland yields the same results, Zavrél does not believe in any specific hormonal influence in this instance, and thinks that among invertebrates only those groups most nearly related to the vertebrates are able to react in a specific manner to the hormones of vertebrates.

Whereas the influence of thyroid preparations upon the development, growth, body-form, and reproduction in Insects must be regarded as still imperfectly analysed, all investigations regarding the action of thyroxine upon the metabolism of the same animals are in agreement. Thus Ashbel (1935) observed an intensified respiration in ova of *Bombyx mori* under the influence of the preparation clyteran, and in the pupae of other Lepidoptera (*Papilio podalirius*, *Vanessa io*, and *Vanessa atalanta*) Romeis & Wüst (1929) and Romeis & Dobkiewicz (1932) obtained the same strong increase of metabolic rate even with very diluted thyroxine solutions. The same phenomenon was observed by Hiestand (1930) and Kocian (1931) in other insect groups (Hymenoptera, Odonata).

2. The Hypophysis

A. **Protozoa.** Nowikoff (1908) and Woodruff & Swingle (1924) used extracts of hypophysis without making a distinction between the different lobes, and tried these extracts on *Paramecium*. They obtained a more rapid rate of fission, whereas Abderhalden & Schiffmann (1922) and Rhodenburg (1930) in similar circumstances got the opposite result and observed a slower division. According to the first-named authors this retardation disappears when after some time the animals have become accustomed to the food, and is then followed by a series of rapid divisions. Ball (1925) and Lwoff (1925) do not regard these results as hormonal but as simply due to the amount of nutrition which is contained in the pituitary extracts. Bramstedt (1937), however, also observed a more rapid rate of fission in *Paramecium* after treatment with the hormone of the posterior pituitary ('Hypophysin-Stark').

B. **Vermes.** Wulzen (1928) fed the flat-worm *Planaria maculata* with pituitary substance and the control animals with liver.

Those worms which had been fed with hypophysis showed a more rapid growth and fission than the controls. Different parts of the gland had the same action upon the rate of fission, but only the anterior lobe acted upon the growth, and this action was restricted to very small individuals.

For the Annelida, Schmidt (1935) and Feuerborn (1936) have investigated the action of the anterior pituitary upon *Lycastis* (cf. p. 5). They found that several different preparations of this part of the gland provoked an unusually early ripening of the eggs, and in this way the action of the gonadotropic hormone of the hypophysis was for the first time established in invertebrates. Hogben & Hobson (1924) did not obtain any evidence of the action of the pressor principle in invertebrates when they tried it on the isolated pharynx in *Aphrodite* in a concentration which would have stimulated the muscles of the mammalian uterus, but Mennicke (1925) was able to demonstrate lively and intensified contractions in the muscles of the earth-worm under the influence of hypophen, comparable with those occurring in the uterus of the guinea-pig after the same treatment.

C. **Echinodermata.** Several pituitary preparations were tried by Ludwig, Ries, & Ries (1935) on the development of the ova in Echinoderms (sea-urchins). The results were, among other things, that the preparation prolan prevented fertilization (which takes place without hindrance in the presence of progynon and pituglandol), and that extracts of placenta, pituglandol, and prolan accelerated cleavage.

D. **Mollusca.** No important results concerning the influence of hypophysis preparations on Mollusca have been published. Hogben & Hobson (1924) were not able to find any influence of pituitary extracts on the crop of snails or the heart of bivalves. On the other hand, Susaeta (1930) reported a retardation of the development in *Barnea* due to the action of pituigan. Finally, the oxytocic principle of the hypophysis may be connected with the expansion of the chromatophores in Cephalopods which Nadler, according to von der Wense (1938), has detected in *Loligo*, for the chromatophores of the Cephalopods are expanded by muscles which are contracted under the influence of adrenaline, thus expanding the pigment-sacs (p. 15).

E. **Arthropoda.** In Crustacea (isolated heart of *Maia*), as in

other invertebrates, Hogben & Hobson (1924) observed no action of hypophysis extracts on muscle contractions, though their concentration was sufficient to stimulate the uterus of Mammals. Hanko (1912), on the other hand, investigated the influence of pituitary extracts on moulting, regeneration, and growth in *Asellus aquaticus*, and in all instances observed a marked stimulation. Abramowitz (1936) succeeded in expanding the chromatophores in the crab *Uca* with intermedin. The same result was obtained by Böttger (1935) in the shrimp *Crangon*. But since the chromatophore reactions are reversed in crabs and shrimps (cf. p. 105), and since, in another shrimp (*Leander adspersus*), Hanström (1937) was not able to find any expansion of the chromatophores under the influence of intermedin, Böttger's result ought to be confirmed.

Only negative results were obtained by Patterson (1928) after feeding insects (larvae of *Sarcophaga saracena* and *Calliphora erythrocephala*) with hypophysis. Patterson used both anterior and posterior pituitary lobes and the whole gland, but could not find any action upon growth or development. On the other hand, Abderhalden (1919) fed larvae of *Deilephila* with pituitary extracts, and among the butterflies bred from these larvae several were strikingly large; in some the body was large but the wings small and abnormally coloured. Thompson (1929) on the contrary found a slower growth, an elongated metamorphosis, and a retarded circulation after administration of extracts of the anterior pituitary to larvae of *Bombyx*. This result was probably due to a lower rate of metabolism, especially of the carbohydrates. In agreement to some extent with these observations, Kotsovsky (1934) was able to prolong the life-span of *Musca domestica* during the autumn with extracts of the hypophysis, whereas the thyroid hormone shortened its life (p. 9). Finally Iwanoff & Mestscherskaja (1935) have found in an interesting investigation that extracts of the posterior pituitary call forth the same changes in the ovaries of mature females of *Blatella germanica* and *Blatta orientalis* as normally occur at the ripening of the eggs, and also take place if unripened ovaries are transferred to the lymph of a mature female. Extracts of the thyroid, thyreoidin, thyroxine, and crystallized iodine on the contrary delay the ripening of the eggs of the Orthoptera investigated. After repeated injections of pituitary

extracts in *Blatta* and *Blatella*, Iwanoff & Mestscherskaja were further able to make animals of the third nymph stage develop into imagines and also to accelerate considerably the time of egg-laying.

3. The Adrenal Gland

A. **Protozoa.** Experiments by Williams & Burge (1927) and Burge, Wickwire, Estes, & Seager (1928) have proved that in unicellular organisms (*Paramecium*) adrenaline is able to play the same part in the carbohydrate metabolism as in higher animals. Very dilute solutions of adrenaline in a concentration of 1: 1,000,000 or 1: 40,000,000 increase the sugar metabolism, whereas more concentrated solutions retard it. Adrenaline also has a slight effect on the metabolism of amino-acids in *Paramecium*. For the influence of adrenaline upon the rate of fission, Rhodenburg (1930) and Medwedewa (1935) have reached contradictory conclusions; the former believes that the hormone stimulates, the latter that it retards the process of fission.

Bauer (1926) and von der Wense (1935) have noted that adrenaline increases the viscosity of protoplasm in *Paramecium* and *Amoeba* and thus checks the mobility, the streaming of the protoplasm, and the pulsations of the contractile vacuoles. According to Bauer (1926), von der Wense (1934, 1935), and Bayer & Wense (1936) this is due to colloid-chemical changes in the protoplasm. Medwedewa (1935) also confirms the decreased activity of the contractile vacuoles under the influence of adrenaline in *Paramecium*, *Amoeba*, and *Vorticella*, and further states that both the cilia and the myonemes show a higher tone. Medwedewa explains the last-named fact by the action of adrenaline upon the neuro-motor apparatus of the Ciliata which functions as a kind of primitive 'nervous' centre in these unicellular organisms (cf. Gelei, 1934, 1935, and Ueymura, 1935). Of interest in this connexion is the statement of von der Wense (1934, 1935) that the action of adrenaline in Protozoa depends on the amount of Ca-ions in the surrounding medium; if this lacks Ca the hormone has no influence upon the protoplasm. The adrenaline is supposed primarily to cause a higher concentration of Ca within the protoplasm, and secondarily an increase of the viscosity and a retardation of the activity of the contractile vacuoles.

B. Coelenterata. Different experiments with preparations of the adrenal glands have thus far only yielded negative evidence regarding their action upon Coelenterates. Schäfer (1921) and Backman (1922) did not obtain any certain evidence of an influence of adrenaline on the muscular contractions of the Scyphomedusae, and May (1926) got the same negative result using extracts of the adrenal gland on the muscles of Actiniae. Medwedewa (1933–6) was further unable to find any influence of adrenaline upon the carbohydrate metabolism in Coelenterata.

C. Vermes. As far back as 1903, Magnus examined the action of adrenaline on *Sipunculus nudus*. He observed that the muscles and the motor-nerves are not directly sensitive to the hormone, but that the whole animal shows typical signs of 'excitement' and later becomes paralysed after injection with adrenaline. Stimulation of a local portion of the ventral nerve-cord with the hormone caused contractions of adjacent muscles, and consequently the point of action seems to be situated centrally and not in the periphery. Neither Gaskell (1920) in *Hirudo* and *Lumbricus* nor Ishigami (1928) in *Lumbricus* were able to show any influence of adrenaline upon the somatic muscles, but Gaskell noticed stronger contractions of the pulsating elements of the vascular system. Concerning some earlier experiments with negative results, Mennicke (1925) lays stress upon the fact that adrenaline really calls forth an increase of the tone in nerveless muscle-preparations of *Lumbricus*; and Hogben & Hobson (1934) also observed an accelerated rhythm of the contractions of the isolated pharynx in *Aphrodite*, both with adrenaline and with the related epinin. Wells (1937) injected adrenaline into the oesophageal region of the coelom of *Arenicola*, and found that it caused the worms to burrow continuously. This is ascribed to the stimulating effect of adrenaline on the oesophageal muscles seen in isolated preparations of oesophagus and proboscis.

Medwedewa (1933–6) has shown that adrenaline has an influence on the carbohydrate metabolism in Annelida.

D. Echinodermata. Only a few scattered papers deal with the action of the adrenal gland upon the Echinodermata. Wyman & Lutz (1930) found that under certain circumstances adrenaline paralyses the cloaca of *Holothuria tubulosa*, and Ludwig, Ries, & Ries (1935) observed that the same hormone in small

quantities accelerates the cleavage divisions in the ova of sea-urchins, but in a stronger concentration retards them; it does not, however, prevent the fertilization of the eggs. Castaldi & Zanco (1935) have noticed that extracts of the adrenal cortex stimulate the early development in *Paracentrotus lividus*.

E. **Mollusca.** A number of investigations are concerned with the problem of the sensitivity of the heart of Mollusca to adrenaline or other adrenal preparations. Whereas Boyer (1926) contends that adrenaline has only an injurious action upon the isolated heart of *Helix pomatia*, causing diastolic stoppage and irregular contractions, all other investigations have consistently shown an increase of the tone of the heart-muscles and of the rhythm of the heart-beats. Thus, among others, Hykès (1929, 1930, 1932) found that the newly hatched larvae of *Pterotrachea mutica* and *Physa fontinalis* are especially sensitive to adrenaline which even in a dilution of 1 : 10,000,000 still brings about an increase of the tone of the heart-muscles, stronger contractions of the heart, and more rapid pulsations. Haberlandt (1930) found the same influence of adrenaline upon the heart of Mollusca as upon that of Vertebrata. Takatsuki (1933) confirmed this observation on the isolated heart of *Ostrea circumpicta*, and Bacq (1933–4) and Jullien (1935) found a limit to the action of adrenaline upon the heart at a dilution $1 : 10^9$, the former in *Ostrea*, the latter in *Loligo pealii*. Bacq observed further that a treatment of the heart of *Loligo* with ergotamin considerably weakened the action of adrenaline, and that solutions of tyramin had an effect qualitatively similar but much weaker.

On other isolated organs of *Loligo* such as the stomach, rectum, oviduct, and penis, adrenaline, according to Bacq (1934), acts in such a manner that the tone of the muscles is increased and their contractions strengthened. The presence of Ca-ions is in this instance not essential for the full action of the hormone. Ungar (1936) and Beauvallet (1936, 1937) have confirmed the observations of Bacq in other Cephalopods (*Sepia*, *Octopus*), and Kruta (1935) found, like Bacq, that tyramin acts in the same manner as adrenaline upon the heart of Cephalopods, though more weakly. Sereni (1928), Bacq (1933, 1934), Nadler (according to von der Wense, 1938), and ten Cate (1933) have observed that the chromatophores in Cephalopods react to adrenaline (cf. p. 11), and Bacq found that ephedrine has a

similar but more prolonged action. According to Lévy & Boyer (1927), ephedrine acts on the heart of snails in a similar manner as adrenaline, just as in many vertebrates. Adrenaline also widens the pupil in Cephalopods (Bacq, 1934).

The influence of adrenaline upon the carbohydrate metabolism in the Mollusca is disputed. Medwedewa (1933–6) believes she has got positive results in *Helix pomatia* (but not in *Anodonta*), whereas Schwarz (1935) and Wolf & Heidegger (1935) deny the action of adrenaline upon the carbohydrate metabolism in the same species. According to the last-named authors the treatment with adrenaline results in a more pallid colour in the animals investigated.

Herwerden (1922, 1923), who also fed Crustacea with the adrenal cortex, examined the influence of this diet upon molluscs, i.e. *Limnaea*, and observed a considerable increase in the growth, reproduction, and resisting power. On the other hand, Chatzillo (1936) found that adrenal optones had no influence upon the growth of the same genus.

F. **Arthropoda.** As early as 1907, Carlson (1907, 1909) discovered that adrenaline has a stimulating influence on the heart of Xiphosura (*Limulus polyphemus*). At a dilution of 1 : 500,000, adrenaline applied to the heart-ganglion still occasions a strong increase in the heart-beats. If applied to the heart-muscles themselves, adrenaline is also active though less strong. The Japanese king-crab, *Tachypleus tridentatus* has also been investigated in this respect by Paik (1934), who found that adrenaline in a dilution of $1 : 10^7$ still actively stimulated the contractions of the heart-muscles. According to Ishihara & Kakei (1935) the heart-rhythm in *Tachypleus* is of neurogenic origin, but if the action of the nervous system is annihilated the heart shows a spontaneous myogenic peristaltic contraction. This is increased by heat and adrenaline, decreased by cold and acetylcholine.

Although Elliot (1905) did not find any influence of adrenaline upon the heart of Crustacea (*Astacus*), and Brücke & Satake (1912) believed they had observed retarded contractions after intravenous injection of adrenaline in *Homarus*, new investigations have yielded results which agree better with those found in the Xiphosura. Thus Hogben & Hobson (1924) and Bain (1929) consistently observed an increased tone and heart-rhythm in *Maja squinado*, *Cancer pagurus*, and *Carcinus maenas*,

even when using very dilute solutions; these authors were not able to detect any retarding action of adrenaline. On the other hand, Fröhlich & Zak (1935) observed a paralysing effect of this hormone upon the digestive canal in Cladocera (*Leptodora*), whilst ephedrine neutralized the action of adrenaline and stimulated the paralysed organ to renewed activity. The chromatophores in *Palaemon* (*Leander*) *squilla* are expanded by adrenaline (Beauvallet & Veil, 1937).

The influence of adrenaline upon the sugar metabolism in Crustacea is as disputed as the results which have been obtained in molluscs in the same field. Thus Medwedewa (1933–6) has also produced hyperglycaemia with adrenaline in Crustacea (*Astacus*), but Kalmus & Waldes (1936) doubt whether this action is specific, since they were able to produce the same effect by injection of several different substances (quinine, insulin, NaCl) into the body-cavity of *Astacus*. Lindblad (1931) and Roche & Dumazert (1935) were, however, unable to observe any influence of adrenaline upon the carbohydrate metabolism in *Astacus fluviatilis* and *Cancer pagurus*.

As in molluscs, an administration of dried adrenal cortex to the aquarium water strongly increases the growth, sexual maturity, reproduction, and resisting power in *Daphnia*: results which could not be obtained with adrenal medulla, liver, hypophysis, or thyroid gland (van Herwerden, 1923). The active principle is soluble in water and withstands boiling, and preparations of adrenal cortex of cows during the first five months of pregnancy were especially active. Banta & Brown (1929) were, however, not able to verify the existence of a specific action of the dried adrenal cortex upon development in Cladocera.

The heart in insects reacts to adrenaline in the same way as that in other arthropods and molluscs. Thus Hykès (1926, 1932) observed a positive chronotropic action of adrenaline in a concentration of 1 : 100,000–1 : 1,000,000,000 in larvae of Chironomidae, and under the influence of the hormone an irregular heart-rhythm was transformed into a regular one.

By feeding larvae of *Deilephila* with partially hydrolysed adrenal substance, Abderhalden (1919) bred butterflies which were of small size and deformed. Farkas & Tangl (1926) report a precocious spinning of the cocoons after injection of adrenaline into the body of *Bombyx* larvae. In the last instance a

simultaneous injection of choline neutralized the action of adrenaline, and a slight retardation of the metamorphosis was obtained. Bray (1929, 1933) fed larvae of Diptera with adrenal cortex and found them heavier than the controls, which were fed with muscle substance; the pupation was delayed, and pupae of larvae which had received adrenal cortex were also heavier than the controls. Medwedewa (1933–6) has also observed a positive influence of adrenaline upon the carbohydrate metabolism in insects in young larvae of *Bombyx*. Older larvae, pupae, and imagines did not react to the hormone.

4. The Pancreas

A. Protozoa. Burge & Estes (1926, 1928), Burge & Williams (1927), Burge, Estes, Wickwire, & Williams (1927), Williams & Burge (1927), and finally Burge, Wickwire, Estes, & Seager (1928) have investigated the action of insulin upon the sugar metabolism in *Paramecium* and among other things they found the following. If Paramecians are cultivated in sugar solutions they absorb considerable quantities of glucose. This glucose consumption is doubled after administration of insulin to the cultures, whereas the hormone has no influence upon the amino-acid metabolism. From their investigations into the role of insulin and adrenaline (cf. p. 13) in the metabolism of Protozoa, these authors conclude that these hormones possess the same functions as in the vertebrate body.

B. Vermes. According to Wulzen & Bahrs (1928), Planarians fed with mashed pancreas are said to show a retarded growth as compared with worms fed on liver. The active substance was not destroyed when heated to 80 degrees C. for 30 minutes.

C. Mollusca. Experiments made in order to test the action of insulin upon the carbohydrate metabolism in molluscs (Collip, 1925, 1927; Schwarz, 1935; Wolff & Heidegger, 1935) have all yielded negative results. Wolff & Heidegger say that individuals of *Helix pomatia* treated with insulin show an especially dark colour compared with those treated with adrenaline (cf. p. 16).

D. Arthropoda. Hemmingsen (1924, 1925), Collip (1925, 1927), Lindblad (1931), and Roche & Dumazert (1935) have examined the influence of insulin upon the carbohydrate metabolism in Crustacea. Collip did not notice any effect on the oxygen consumption, and Hemmingsen, Lindblad, and

Roche & Dumazert observed no reduction in the amount of blood-sugar, nor any of the striking symptoms normally following hypoglycaemia and leading to coma. Hemmingsen also investigated insects, namely larvae of *Sphinx* and *Deilephila* and pupae of *Smerinthus*, without any positive results. Medwedewa (1933–6) had the same result from experiments on *Bombyx mori*. In the same material (larvae of *Bombyx*), Wenig & Joachim (1935) found, however, that after an injection of 1/10 clinical unit of insulin the glucose disappears from the body-fluid, whereas the total amount of reducing substances in the blood (of which the glucose represents about 25 per cent.) remains unchanged. The difference in these results calls for further study.

5. The Thymus

Abderhalden & Schiffmann (1922) ascribe to extracts of thymus a stimulating influence on fission in *Paramecium*. Lwoff, however (1925), does not admit in this case a specific reaction to the extracts, but regards the effects as due to the nutritive value of the preparations. Shumway (1914, 1917, 1929) found, contrary to Abderhalden & Schiffmann, that thymus extracts retard the rate of fission in *Paramecium*, but Enriquez (cf. Capua, 1931) maintained that this was only true at the start of the experiments since later on more rapid fission took place.

During his many experiments with the Polychaete annelid *Lycastis*, Schmidt (1935) found that the thymus preparation thymus-dispertpulver (Krause, *Med. Ges.*) had partly the same effect as thyroid preparations, viz. an earlier formation and ripening of the ova. Compared with the thyroid animals, the thymus animals seemed to be fatter and looser and the blood colour was different.

Chatzillo (1936) observed that thymus optones retarded growth in molluscs (*Limnaea stagnalis*). According to Abderhalden (1919), insect larvae (*Deilephila*) fed on thymus gave rise to butterflies with more pallid fore-wings, and Zavrel (1930, 1931) observed a probably non-specific effect of thymus feeding on the growth of larvae of Chironomidae (cf. p. 10).

6. The Gonads

According to Abderhalden & Schiffman (1922) and Rhodenburg (1930), extracts of testis promote fission in *Paramecium*, but

the latter author did not find any such influence of extracts of the ovaries, and the former report that extracts of the corpus luteum retard the rate of fission. Lwoff (1925) maintains that the results obtained by Abderhalden & Schiffmann are due to the nutritive value of the extracts used.

The investigations of Schmidt (1935) on *Lycastis* also comprised an examination of the influence of the follicular hormone preparation perlatan and of progynon upon this polychaetous worm. These experiments yielded negative results, according to Schmidt because the annelids do not possess organs which can react to these vertebrate hormones. Visnak (1935) also tried crystallized follicular hormone on the Oligochaeta *Eisenia foetida* and *Rhynchelmis limosella* without being able to notice any influence upon the sexual characters or reproduction. In agreement with this, Dantchakoff & Vachkowitchuté (1936) observed no action of folliculin on male larvae of *Drosophila* and no action of progynon on female larvae. The sexual characters in insects seem, furthermore, to be genetically and very firmly determined, so that the possibility of affecting them with vertebrate hormones was not very great from the start (p. 43).

7. Other Vertebrate Hormones

Extracts of the pineal gland stimulate fission in *Paramecium* according to Woodruff & Swingle (1924).

Parhon & Parhon (1931) are among those scientists who vindicate the importance of hormonal reactions in invertebrates, and Parhon & Derevici (1932) found that the concretions inside the stomach of *Astacus* lost in weight after injections of parathormone from the parathyroid, but afterwards contained relatively more calcium.

Serfaty (1934) and von der Wense (1935, 1937) have investigated the influence of choline and acetylcholine on Protozoa (*Stylonychia* and *Paramecium*). Both authors found a considerable sensitivity to these substances, and von der Wense was also able to show that the antagonistic action between the sympathomimetic adrenaline and the parasympathomimetic choline which is found in vertebrates can also be observed in Protozoa. Choline was more active than acetylcholine, and, contrary to adrenaline, stimulated the pulsation of the contractile vacuoles and the swimming movements. This action

was independent of the concentration of H-ions in the solutions.

Several other invertebrate groups have also been tested for their sensitivity to acetylcholine. Thus Fühner (1918; cf. Ishigami, 1928) found that a nerveless muscle-preparation of the leech (*Hirudo*) still reacts to acetylcholine in a concentration of 1 : 1,000,000, and that the sensitivity is increased a thousandfold after a preliminary treatment with physostigmin. This pharmacologically important result has been further investigated and developed by Kahlson & Uvnäs (1935), Bayer & Wense (1935, 1936), and others (cf. von der Wense, 1938). For the Mollusca, too, several investigations on the influence of acetylcholine upon different organs have been published, e.g. by Jullien & Morin (1931), Morin & Jullien (1932), ten Cate (1933), Bacq (1933, 1934, 1935), Gautrelet & Halpern (1935), Jullien (1935, 1937), and Ungar (1936). Here also, acetylcholine and adrenaline often, but not always, act antagonistically. Thus adrenaline increases and acetylcholine decreases the activity of the mollusc heart, and the former substance, according to ten Cate, contracts, while the latter expands, the chromatophores in Cephalopods. In Arthropods, i.e., the Xiphosura *Limulus polyphemus* and *Tachypleus tridentatus*, the same hormones act in an antagonistic manner (Paik, 1934; Ishihara & Kakei, 1935). In *Arenicola*, however, Wells (1937) was unable to find any certain evidence of an antagonistic action of acetylcholine on the contraction of the oesophagus and proboscis (cf. p. 14). Other investigations on the action of acetylcholine in Arthropods are reviewed in Bacq (1935) and von der Wense (1938), among them that of Bonnet (1937), who examined the antagonistic action of acetylcholine and strychnine upon *Astacus*. (Cf. also Welsh, 1938.)

Finally, it may be mentioned in this connexion that the growth hormone of plants, auxin, stimulates the divisions of the flagellate *Euglena viridis* (Popoff, 1933), and that extracts of root-tips promote fission in *Paramecium* (Dimitrowa, 1935). On the other hand, Kropp & Crozier (1934) and Navez & Kropp (1934) say they have detected substances in the eye-stalks of Crustacea (*Palaemonetes vulgaris*) which, like the plant auxins, stimulate the growth of decapitated root-tips of *Avena* and retard the growth of the same organs in *Lupinus*.

II

THE INFLUENCE OF INVERTEBRATE HORMONES ON VERTEBRATES

WHEREAS numerous investigations which have been reviewed in Chapter I deal with attempts to apply our knowledge of vertebrate hormones to invertebrates, or to detect new appropriate test-objects for pharmacological experiments among the latter animals, relatively few scientists have tried the action of invertebrate hormones on vertebrates. The first of them was Biedl (1912). Since some earlier investigators had detected the presence of chromaffine cells in the ventral nerve-ganglia of *Hirudo* and other annelids (p. 142), Biedl extracted from these ganglia a substance which had the same properties as adrenaline and, according to Biedl, was identical with this hormone. A substance with the same properties has since been found also in Protozoa.

The experiments of von der Wense on the antagonistic and in several respects very important actions of adrenaline and choline in unicellular organisms led him to believe that these substances normally occur in Protozoa and play a part in their vital processes. Researches by Bayer & Wense (1935, 1936) showed that this was the case. From several litres of hay cultures some millions of Paramecians were centrifuged and then broken up by repeated freezing and thawing. The lipoids were dialysed, and in the residue three different substances were proved to exist, which corresponded to adrenaline, choline, and acetylcholine. The adrenaline reaction was tried on the isolated frog-heart and the alimentary canal of the rabbit with a positive result, and like adrenaline this substance was inactivated by oxygen. The occurrence of acetylcholine and choline in the *Paramecium*-extract was proved by means of the nerveless muscle-preparation of *Hirudo* (p. 21) and the isolated frog-heart, and their normal physiological importance in Paramecians was made probable by the detection by von der Wense (1937) of a ferment in the protoplasm of Paramecians which decomposes acetylcholine.

In extracts of the tentacles of Coelenterates (*Hydra*) Koshtojanz & Mitropolitanskaja (1936) have found a substance of the

same nature as adrenaline, and a similar substance in the cerebral ganglia of *Helix pomatia*. In other molluscs Dubois (1907) and Roaf & Nierenstein (1907) have detected a substance of the same kind. This was extracted from the purple gland of *Murex brandaris* by Dubois and from the hypobranchial gland by Roaf & Nierenstein, who tested it with a positive result on the contractions of the blood-vessels in the frog and on the blood-pressure in the rabbit. In a histological investigation Roaf found chromophil (chromaffine) cells in the purple gland, but he hesitates, however, to claim the incretory function of these cells, while Lison (1932) regards them as 'pseudochromophil' cells. Finally, Henze (1913) has found in the salivary glands of Cephalopods *p*-oxyphenylethylamin (tyramin), which is also present in the blood, and is chemically and pharmacologically closely related to adrenaline.

From leeches (*Hirudo medicinalis*) and insects (*Tenebrio molitor*) von der Wense (1938) has extracted a substance which shows the same physiological action upon the isolated frog-heart and the intestine of the rabbit as adrenaline. From larvae of *Tenebrio* he also succeeded in producing a crystalline substance according to the recipe for extracting adrenaline from the adrenal gland in vertebrates, and this substance had the melting-point of adrenaline and showed most of its biological and physico-chemical properties. In the same species of insects Raper (1926, 1927) has proved the existence of 3,4-dioxiphenylalanin, which is the mother substance of adrenaline.

The acetylcholine which was found by Bayer & Wense in Protozoans has also been detected in several other invertebrates. Thus Bacq (1935) found it in *Sipunculus*, *Halla*, and *Spirographis*. Further, in *Sipunculus*, in Echinoderms and in Molluscs, he found a ferment which decomposes acetylcholine. Bacq (1935) also detected the presence of acetylcholine in the Mollusca (*Octopus*, *Aplysia*, *Pedunculus*), in which group it was later found by Mentzner, Kaswin, Corteggiani, & Gautrelet (1936) in *Helix pomatia*. In *Octopus vulgaris*, which contains relatively large amounts of the substance in its central nervous system, Bacq & Mazza (1935) succeeded in producing a pure crystallized chemical compound of acetylcholine and gold chloride.

In Crustacea, acetylcholine was again detected by Bacq (1935) in *Maja* and *Penaeus*, and Marnay & Nachmansohn (1937)

found the ferment which is able to decompose it. This ferment was found to be present in the ventral ganglia of *Homarus* in a concentration which was 100 times stronger than in the muscles, and hence Marnay & Nachmansohn conclude that it must play a part in the function of the nervous system of Crustacea.

Not only are adrenaline, acetylcholine, and choline present in the protoplasm of Protozoa, but according to Steidle (1930) and Bauer (1932) there are also substances which are able to produce oestrus in mammals. Thus Bauer extracted with alcohol from large amounts of *Colpoda steini* a substance which had similar properties to the folliculin of mammals, and produced oestrus in castrated female mice. Wense (1938) has also tested Paramecians for the presence of sexual hormones but with negative results, and believes that this was due to starting the investigation with too small amounts of material.

Substances which produced oestrus in mammals were found in Echinoderms by Steidle (1930) and Donahue & Jennings (1937). Steidle tested the sperm and ova of *Echinus miliaris*, and Donahue & Jennings the ovaries of *Lytechinus variegatus*, with positive results; the last experiment especially showed the presence of a strong oestrus-producing substance. In his comprehensive paper Steidle (1930) investigated still other groups of invertebrates, i.e. Nematoda, Cestoda, and Oligochaeta, finding oestrus-producing substances in representatives for all these worms and in the Mollusca *Aplysia*, *Octopus*, and *Eledone*. Schwerdtfeger (1931), however, was not able to show the presence of this substance in the Mollusc *Chiton marginatus*, but got positive results upon castrated female mice with aqueous extracts from the Coelenterate *Actinia equina*, from insects (*Vespa crabro*), and from spiders. From bees, spiders, and scorpions Steidle (1930) extracted oestrus-producing substances which during certain periods of sexual development exist in very small quantities and on the whole show a variable occurrence. Of considerable interest is the quantitative determination of the amount of oestrus-producing substance in the ovaries and oviducts of the moth *Attacus atlas* which was made by Loewe, Randenbusch, Voss, & van Heurn (1922), and was found to be equivalent to the amount found in the corresponding organs of mammals.

Stefani (1931) injected extracts from larvae and pupae of

Bombyx mori into pregnant guinea-pigs from which the uterus had been extirpated, and examined the influence upon the ovaries. He found that the injections prevented the involution of the corpus luteum, because a month after the beginning of the injections the ovaries still appeared as if they had been treated with extracts of vertebrate embryos. Consequently larvae and pupae of insects contain a substance which has a morphogenetic influence upon the corpus luteum of pregnancy.

The common—or perhaps regular—occurrence of the oestrus hormone (oestrin, folliculin, thelykinin, or progynon) in invertebrates suggests that this substance may be of physiological importance to the invertebrates themselves. Loewe, Randenbusch, Voss, & van Heurn (1922) have considered the following three possibilities in an attempt to explain its occurrence: (1) the occurrence of the oestrus-producing substances in invertebrates may be accidental, and of no physiological importance; (2) the hormones might have a different function in invertebrates and in vertebrates and might perhaps be used as hormones; and (3) they really function as sexual hormones also in invertebrates. Hypothesis no. 3 is not favoured by the fact that almost all experiments in this field have proved the absence of a hormonal regulation of the sexual functions in insects (in which the oestrus-producing substances have been found in so many instances); besides, substances with the same physiological action have been detected in different parts of plants, such as flowers, roots, and yeast-cells, and even in peat. In the other direction Wasicky, Brandner, & Hauke (1933) have shown that several animal hormones, such as sexual hormones and extracts of the anterior pituitary and the thyroid, promote the florification of plants.

In still another field there exist several instances of an influence of invertebrate hormones on vertebrates, viz. in colour-change. Koller & Meyer (1930), Meyer (1930, 1931), Perkins & Kropp (1932), Kropp & Perkins (1933), and Abramowitz (1936) have all examined the action of the Crustacean eye-stalk hormone (which regulates the colour-change in these Arthropods) on the chromatophores of vertebrates. Just as the intermedin of the vertebrate hypophysis is able to act upon the crustacean chromatophores (p. 12), so the colour-change hormone of the latter has an influence upon the pigment expansion

of vertebrates. The papers of different authors conflict in certain respects, but Abramowitz obtained consistent results under particular experimental conditions for the different groups of vertebrates: the extracts of the eye-stalks of *Palaemonetes vulgaris* always expanded the melanophores of hypophysectomized sharks (*Mustelus*), of white-adapted and hypophysectomized frogs and tadpoles (*Rana pipiens*), and of white-adapted and hypophysectomized lizards (*Anolis carolinensis*), increased the expansion of the melanophores of hypophysectomized catfish (*Ameiurus nebulosus*), and expanded the melanophores and erythrophores in the bony fish *Chrosomus erythrogaster*. In these respects it is not unreasonable to compare the colour-change hormone of the Crustacea with the intermedin of vertebrates with which it also agrees in certain other respects (p. 108), though at present there is no reason to believe that these two hormones are chemically identical.

III

SEX HORMONES. THE EFFECTS OF PARASITIC AND EXPERIMENTAL CASTRATION IN INVERTEBRATES

AS Koller (1929) has pointed out in the first comprehensive paper on the hormones of invertebrates, it was the problem whether a correlation exists between the gonads and the secondary sexual characters that first led to the hypothesis of the occurrence of hormonal reactions in invertebrates. This problem is intimately connected with the question of the origin of intersexes, and with the consequences of parasitic castration (which has been known a long time) and of experimental castration, which has been used in modern zoology during recent years.

In some Nematoda intersexes are so common (Steiner, 1923; Cobb, Steiner, & Christie, 1927; Comas, 1927; Goldschmidt, 1931) that according to Steiner no other animal group is known in which this phenomenon occurs more often. In these instances

the males, females, and intersexes are found in very characteristic circumstances. Thus in *Paramermis contorta*, which lives in larvae of *Chironomus thummi*, the greater number of animals are males if more than five parasites occur in the same host; if the host contains but one parasite this is in 155 instances out of 272 a female. If the number of parasites in the same host is less than five and greater than one, several intersexes will be found together with normal males and females (Caullery & Comas, 1928). It seems not improbable that hormone-like reactions play a part in the sex-determination of these Nematodes.

It must be observed that the term 'parasitic castration' is not used here in a literal sense. In all cases of so-called parasitic castration the parasites are injurious to the gonads, but only very rarely do they completely destroy them. Thus in many instances of parasitic castration the gonads contain normal sexual products in the genital glands, though in reduced proportions.

Whereas in some instances of parasitic castration in Turbellaria (*Leptoplana*) and Nemertina (*Lineus obscurus*) Giard (1888) was unable to notice any alteration of the secondary sexual characters, Vandel (1920, 1921) established experimentally the existence of a connexion between the gonads and the external sexual characters. Thus after different operative interferences he showed that the regeneration of the copulatory apparatus in Planarians is dependent upon the presence of the gonads, especially the testes.

A much-discussed instance of sexual development in worms is the *Bonellia*-problem (Spengel, 1879; Baltzer, 1914–33; Goldschmidt, 1920, 1926, 1931; Seiler, 1927; Herbst, 1928, 1929, 1932, 1935, 1936; Michel, 1930; Glaus, 1933; Nowinski, 1934; Heydenreich, 1935; Loosli, 1935; Mutscheller, 1935). According to the principles laid down in the introduction to this book (p. 2) I should not have dealt with the *Bonellia*-problem here, but since it has often been treated together with hormonal reactions in invertebrates, I think there is reason to give a short review of it in this connexion.

The difference between the sexes in *Bonellia* (Fig. 1) is very great, since the body of the female is as big as a plum and is supplied with a proboscis of a length of about 3 feet, whereas the male is very small (a few millimetres), not unlike a Planarian, and lives within the body of the female (Fig. 1). In early

development all larvae are alike, but after a time some of them adhere to the proboscis of a female, where they stay for three days and then in a few days develop into the dwarf males. The remaining, free-swimming, larvae after some time sink to the bottom and mostly develop into females. If the larvae which are attached to the proboscis of the female are violently removed before the end of three days they develop into intersexes, but on the other hand, the attachment to the proboscis can be experimentally compensated for by a treatment with an extract from the proboscis or other portions of the female body. Thus Baltzer concludes that male-activating substances are produced by the female and transferred to the larvae, retarding the development in the female direction and rendering the larvae neotenic. The active substance is water-soluble, is not destroyed by boiling, and does not contain albumen.

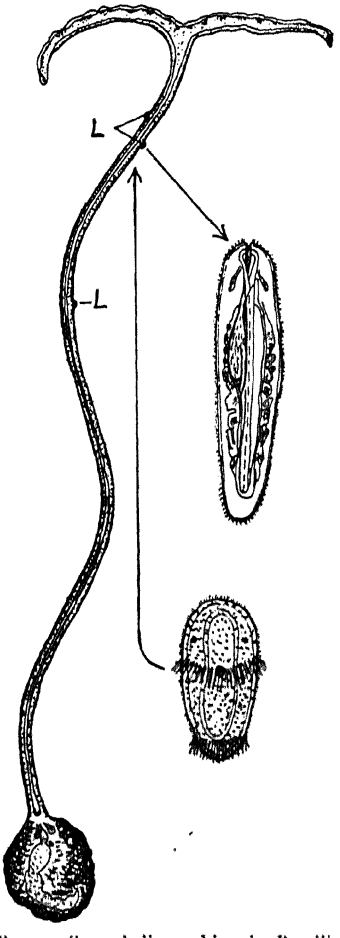


FIG. 1. Sexual dimorphism in *Bonellia viridis*. Mature female and male and indifferent young larva. *L* attached larvae. After Baltzer.

Investigations by Seiler (1927), Herbst (1928–36), Heydenreich (1935), and Mutscheller (1935) lead to a different conclusion regarding the development of sex in *Bonellia*. These authors have found that the unattached, free, and indifferent larvae develop in a male or female direction under the influence of certain chemical agencies. Thus a change of p_H after addition of CO_2 or HCl acts in a male direction, whereas K- and Mg-ions act in a female direction.

If the normal amount of K in the water is doubled or trebled the indifferent larvae again develop into males, but an abnormal increase of Mg does not act in the same manner. These experimental results do not, however (Baltzer, 1932, 1933; Glaus, 1933; Nowinski, 1934), exclude the possibility that a substance which in several respects acts like a hormone produced by the female and determines the sexual development of the attached larvae. According to Baltzer (1932) the sexual development in *Bonellia viridis* may be determined in three or four different ways: (1) a genetically determined female development; (2) a genetically determined male development (the action of the male-determining genes would be weaker than that of the female-determining, and these larvae develop into imperfect males, 'Spätmännchen', without ripe sperms); (3) a development in a male direction under the influence of the substances from the female proboscis; and (4) a development in a male direction under the influence of factors in the surrounding medium. (Cf. Baltzer, 1937).

The resemblances between the hormonal reactions in vertebrates and the influence of the female *Bonellia* upon the larvae which have been pointed out by Baltzer (1932) and Nowinski (1934) demand in any case an extension of the common definition of a hormonal process. But, according to Hartmann & Huth (1936), Baltzer's conclusions regarding the imperfect males ('Spätmännchen') are not imperative. The last-named authors have investigated the sexual development of the polychaetous annelid *Ophryotrocha* and are of the opinion that in both *Bonellia* and *Ophryotrocha* sex is phenotypically determined; in both, the juvenile stage is male, the adult female, in structure, and in both instances substances from the adult female (in addition to other factors) act in a male direction.

In earth-worms there is a type of parasitic castration which probably acts on the development of the secondary sexual characters, i.e. the clitellum (a thickened portion of the epidermis with glands and blood-vessels, comprising segments 32 to 37). The clitellum shows cyclical changes in connexion with reproduction, being active during copulation and supplying the material for the egg cocoons. Sollas (1911; cf. also Hessel, 1909) observed several *Lumbricus herculeus* (*L. terrestris*) which lacked the clitellum and in which the testes, but not the ovaries,

were destroyed by parasitic Monocystoidea. Starting from this observation, Harms (1912) extirpated the segments which contained the testes or the ovaries and observed the influence of the operation upon the development of the clitellum. He found that after extirpation of the testes the clitellum was either reduced or did not develop at all, whereas extirpation of the ovaries did not affect its development. In spite of the agreement between the observations of Sollas and the experiments of Harms, Avel (1928, 1929) was not able to confirm Harms' results in experiments with *Allolobophora* (*Lumbricus*?) *terrestris* and *Allolobophora caliginosa*. With improved methods Avel succeeded in keeping the experimental animals alive for two and a half years after the operation, which involved either total castration or extirpation of the ovaries or the testes. Avel was not able to observe any influence of the gonads on the clitellum, and found that totally castrated animals copulated in a normal manner. A regeneration of the gonads during the experiments was only exceptionally observed. Though Avel does not completely deny the possibility of a hormonal action of the gonads, he clearly showed that the development of the clitellum must chiefly depend upon the nutritive condition of the animals.

The contradictory results of Harms (1912) and Avel (1928, 1929) were in part reconciled by Heumann (1931), who at first stated that oogenesis has no connexion with the development of the clitellum. This development takes place in two stages, the first of which is simultaneous with the spermiogenesis in the beginning of the reproductive period, whereas the second occurs later and culminates in the completely developed organ which can be easily observed externally. According to Heumann, the first stage of the development of the clitellum and the spermiogenesis can be traced back to a common origin, the hypothetical 'superior factor' of Avel, whereas the second stage might be connected with a hormonal influence of the ripened sperms.

In this connexion it is of interest that Brasil (1905), Depdolla (1906), and Dehorne (1923) believe that they have found certain cells in the testes of *Lumbricus* and *Stylaria* which would correspond to the interstitial cells in the vertebrates. But Stieve & Beykirch (1934) were not able to confirm this statement in *Lumbricus herculeus* and *terrestris* (synonymous?), and thus if there is an internal secretion from the gonads (which they think very

probably exists), it must be produced by the spermatocytes or, according to Heumann, from the ripe sperms.

2. Echinodermata

In Echinoderms, too, the gonads may be more or less completely destroyed by internal parasites (Fewkes, 1888; Giard, 1888; Fisher, 1911–30; Brattström, 1936). When specimens of the Cirripede Crustacean *Ulophysema öresundense* which lives within *Echinocardium cordatum* grow big, some or all of the gonads of the host wither away. Although most Echinoderms (including *Echinocardium*) are normally not hermaphrodites but dioecious, no secondary sexual characters exist (only a difference in size; cf. Okshima & Ikeda, 1934), and thus it is not possible to draw any conclusions regarding the existence of sex hormones in this instance of parasitic castration.

3. Mollusca

Several instances of parasitic castration in molluscs (*Paludina*, *Limnaea*, *Planorbis*) are mentioned in the paper by Giard (1888), who could observe no influence upon the secondary sexual characters. According to Linke (1934) (cf. also Linke, 1935), however, there exists a connexion between the gonads and other sexual organs in *Littorina littorea*, since the organs belonging to the genital system, among them the penis, were reduced after the gonads had been more or less destroyed after infection with Trematoda. The connexion between the gonads and the secondary sexual characters can also be observed during the normal sexual rhythm of *Littorina*, since the development of the penis and the accessory sexual glands seems to be correlated in time with the evolutive and involutive phases of the gonads during the yearly sexual cycle.

In the Cephalopods, Sereni (1929) has practised experimental castration and shown that the development of the secondary sexual characters, especially the copulatory organ (the hectocotylus), depends upon the presence of the gonads.

4. Crustacea

Parasitic castration in higher Crustacea commonly takes place under the influence of those curious lower Crustacea, the Rhizocephala, belonging to the Cirripedia. Sometimes also

parasitic worms belonging to the Acanthocephala have been found in the interior of Crustaceans influencing the development of the sexual organs. Thus Roux (1931) found *Polymorphus minutus* parasitic in the body-cavity of *Gammarus pulex*, where it retarded the growth of the ovaries and especially the development of the yolk. The infected females did not show any reproductive activity, and the oostegites of their legs did not carry any marginal bristles, which in normal females hide the eggs. The author was at first unable to decide whether this fact was due to the lower general metabolism or the retarded development of the ovaries, but later solved the problem experimentally (p. 40).

In some comprehensive papers of recent years (Koller, 1929, 1937; Goldschmidt, 1931; Tucker, 1931; Brinkmann, 1936) the meaning of the changes which take place in the organism of decapod Crustacea under the influence of parasitic Rhizocephala is discussed. The literature on this subject is very copious and cannot be fully reviewed here (cf. Giard, 1886–1904; Smith, 1906, 1910; Potts, 1906; Guerin & Ganivet, 1911; Robson, 1912; Biedl, 1913; Courrier, 1921; Harms, 1914, 1926; Lipschütz, 1924; Nilsson & Cantell, 1926; Perez, 1927, 1929, 1932, 1933, 1934; Salt, 1927; Fischer, 1927, 1928; van Oordt, 1928, 1929; Meisenheimer, 1930; Tucker, 1931; Turner, 1933; Day, 1935; Hiro, 1935; Okada & Miyashita, 1935; Drilhon, 1937, and Forsman, 1938).

The young of the Rhizocephala is hatched as a nauplius larva and later passes into a free-swimming cypris-stage. After a brief free existence it attaches itself to the body of its host, commonly a young decapod Crustacean (often a crab). During reduction of the locomotor organs and sense organs, the parasite is converted into a round sac-like mass which absorbs its nutriment from the host by means of root-like threads; its only function is growth and reproduction. The connexion between the parasite and the host is so intimate that in many instances it is difficult to tell which portions of the tissues belong to one or the other. Through phagocytosis the parasite destroys the tissues of its host, especially the connective tissue and the gonads, and absorbs the nutriment without killing it.

Ever since Giard's work it has been known that male crabs infected by Rhizocephala (*Sacculina*) develop in a female direc-

tion, as shown by changes in the claws, the pleopods, and the form of the abdomen, while the testes are more or less degene-

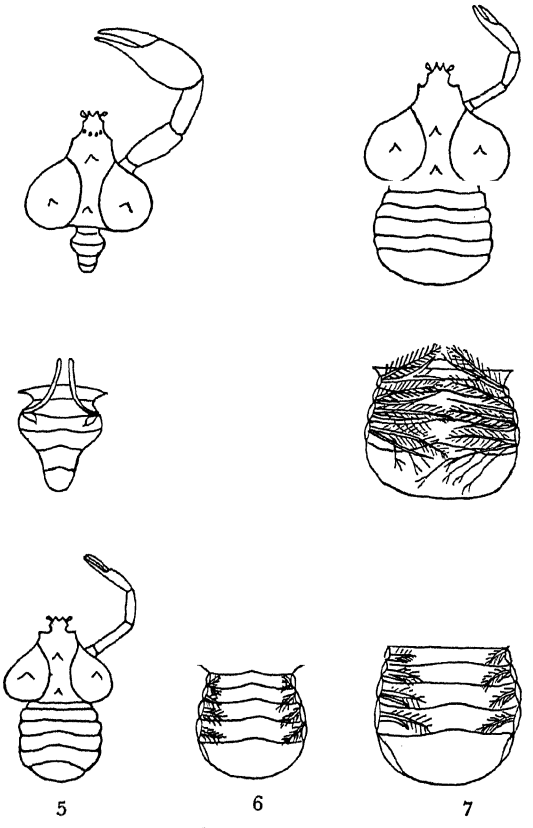


FIG. 2. The crab *Inachus*. 1, normal male with short small abdomen and broad claw; 2, male abdomen without pleopods from beneath; 3, normal female with broad abdomen and small claw; 4, female abdomen from beneath with hairy pleopods; 5, sacculinized male with female characters (small claw and broad abdomen); 6, abdomen of sacculinized male from beneath with pleopods; 7, abdomen of sacculinized female. After Smith.

rated (Fig. 2; cf. Fig. 4). Infected females on the contrary show no or very unimportant changes. Giard explains these facts as due to a retardation of development owing to the low rate of

metabolism, the cause of which is the parasite. According to Smith, however, there exists in Decapods a 'sexual-formative' substance acting both on the development of the gonads and on that of the secondary sexual characters, which latter would thus not show any influence of the action of the former. The sexual-formative substance would act through the agency of the fats which occur in the blood and liver of the crabs. The rhizocephalan *Sacculina*, Smith continues, should increase the amount of fat in the infected males and thus exert a feminizing action upon these analogous with the influence of the ripening of the ova in the females.

Biedl has published an explanation, simple in hormonal respects, of the changes which occur in 'sacculinized' males. Through the action of the parasite the gonads of the host are completely or partially destroyed and their hormonal activity injured or inhibited. In addition, the parasite acts as a transplanted female gonad, since, according to Biedl's opinion, all individuals of *Sacculina* ought to be females. With this view Harms concurred, whereas van Oordt and Goldschmidt objected that *Sacculina* was a hermaphrodite. Koller, who in 1929 disagreed with Biedl, in 1937 lays stress upon the incompletely known sexual functions in *Sacculina*, but admits that there is at least a slight possibility that the parasite possesses a hormonal influence upon its host.

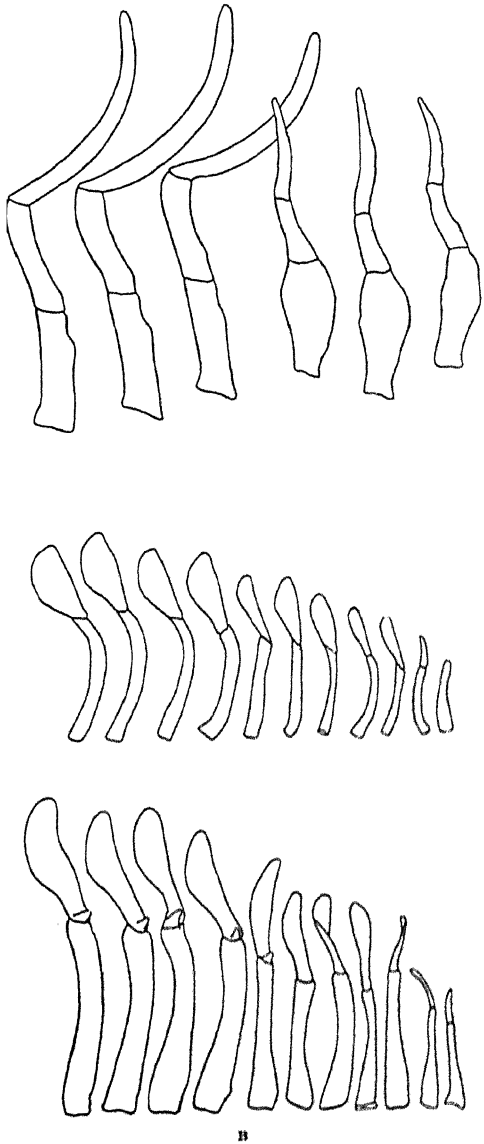
According to Lipschütz and van Oordt, the sacculinized males of crabs represent 'a neutral form' which has adopted female characters to a certain extent. The direction of the female development would according to this hypothesis be predetermined and the males would have developed in the same direction if the hormones of the testes had not intervened during growth and changed the development in a male direction. As a result of castration the action of the male hormones is reduced or inhibited, and more or less accentuated female characters are automatically produced in the infected males.

Goldschmidt founds his opinion on the almost generally accepted absence of sex hormones in insects, and hence denies their presence in the nearly related Crustacea. He therefore regards all changes which are brought about in the Decapoda by the presence of the parasitic Rhizocephala as examples of intersexuality, the special characters of which depend on the

'formative sexual substances' produced by the sex genes. So-called 'zygotic intersexuality' is produced if the hormones of the opposite sex become the more active during later stages of the development on account of an abnormal gene-constitution; 'parasitic intersexuality' is produced when the parasite damages its host in such a manner that the action of the formative sexual substances is abnormally changed.

The latest experimental investigations in this field show, however, that sex hormones really exist in Crustacea, an opinion with which Brinkmann (1936) agrees as a result of his investigations into the influence of Rhizocephala on the secondary sexual characters in Norwegian species of *Munida*. Of the three species of Rhizocephala examined by Brinkmann, *Triangulus munidae* occasions a total atrophy of the gonads, i.e. a real castration, whereas *Lernaeodiscus ingolfi* produces a morphologically partial atrophy, and *Triangulus boschmai* only reduces the amount of ova and sperms produced by the host.

In *Munida sarsi* an infection by *Triangulus munidae* (Fig. 3 B) causes a strong reduction of pleopods 1 and 2 in the males in which they function as copulatory organs, and therefore are normally powerfully developed. On the other hand, pleopods 3, 4, and 5, which have no function in the males and therefore normally are feebly developed, in infected males grow and become differentiated as in the females, in which they are used to carry the brood. Brinkmann contests Goldschmidt's statement regarding the absence of sex hormones in Crustacea, and explains the above-mentioned facts in the following manner; to some extent in agreement with Lipschütz and van Oordt. In the Crustacea there is a male sex hormone the presence of which prevents the development of the pleopods in a female direction, but the absence of which allows this. To complete the picture a more or less extreme condition of hyponutrition is necessary, with the pleopods developed in reduced form on account of the presence of the parasite. The postulated male hormone which under normal conditions prevents the development of the pleopods in a female direction in males is lacking in females. The parasitic atrophy of the ovaries has therefore no influence on the pleopods in females. They metamorphose as usual, but their lower general metabolism causes a slower metamorphosis and more or less feebly developed



B

FIG. 3. A. To the left normal female pleopods 3–5 of *Munida sarsi*; to the right the same pleopods of a male *Munida sarsi* which was infected with *Lernaeodiscus ingolfi*. B. In the upper row male pleopod 2, in the lower row male pleopod 1 of *Munida sarsi*. The left pleopod in both rows belongs to a normal animal; the other ten pleopods belong to animals infected with *Triangulus munidae*. After Brinkmann.

pleopods which resemble the pleopods of infected males which have developed in a female direction.

The influence of *Lernaeodiscus ingolfi* upon *Munida sarsi* (Fig. 3 A) shows roughly the same picture as that of *Triangulus munidae*, whereas an infection with *Triangulus boschmai* has no influence on the secondary sexual characters of its host, though it is the biggest of the rhizocephalan parasites investigated by Brinkmann and must also have the biggest claim on the nutrition. Contrary to the two first-named rhizocephalan parasites, *Triangulus boschmai* does not bring about castration in the host, and thus it is not only the claims on the nutrition (which factor Tucker and Smith believe to be the most important) that can be held responsible for the changes which occur in the infected male crabs. Other factors too must play a part, and, according to Brinkmann it is necessary to reckon with three different processes which can occur simultaneously, or separately, or else not at all. The first is the castration of the host, which is brought about by substances which are produced by the parasite and transferred into the blood of the host. Thus, Perez has shown (1934) that *Sacculina* increases the rate of atrophy in the ovaries of *Macropodia rostrata* which normally occurs during the involutary phases of the sexual cycle. This atrophy is brought about by means of phagocytic digestion of the most mature oocytes. The second factor active in parasitic castration is the consequences of the lower metabolism of the crab, and the third is the absence of the sex hormones of the host as a consequence of castration. This latter factor has only been shown to occur in the males, since the changes which are found in the infected females can be explained as a consequence of scanty nutrition. In the males, pleopods 3–5, which have no function and normally remain at the same stage as in sexually immature animals, develop after the atrophy of the testes in a female direction (cf. Fig. 4). By a combination of the effects of the absence of the male sex hormone (which promotes the development of male and prevents the development of female characters) and the more or less strongly pronounced consequences of a lower general metabolism, Brinkmann explains all changes in the secondary sexual characters which can be observed in decapod Crustacea after parasitic castration with Rhizocephala.

In the Japanese wool-hand crab (*Eriocheir japonicus*) Okada & Miyashita (1935) have, however, recently detected an instance of very far-reaching changes under the influence of parasitic castration by *Sacculina gregaria*. In the most extreme instances no trace of the male copulatory organs, the gonopods, could be found in feminized males of *Eriocheir japonicus*, whereas four pairs of fully developed female pleopods were present. According to Smith the root-like threads of *Sacculina neglecta*, through which

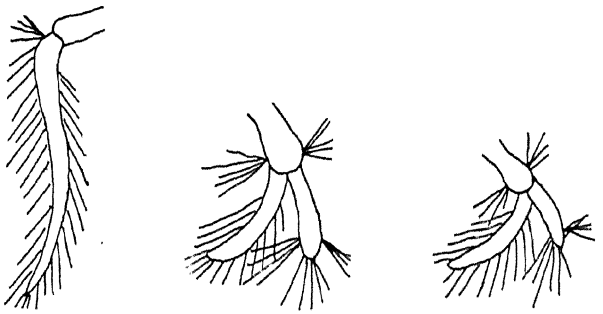


FIG. 4. Third pleopod of *Anapagurus chiroacanthus*. A normal male (exopodite only); B normal female (both exopodite and endopodite); C male, which was infected with *Peltogaster* (exopodite and endopodite). After Nilsson-Cantell.

the nutriment is absorbed, penetrate into the ovaries of *Inachus mauretanicus* but not into the testes. In *Eriocheir japonicus* the same threads are found only seldom in the ovaries but grow into the testes in large quantities, and even break up their tubules into sections. In spite of these injuries, normal spermatocytes and sperms can be found in the detached tubules. In some of the infected males Okada & Miyashita even detected a 'complete sex-reversal'. Though the parasite still remained within the body of the crab, two of these original males possessed hermaphrodite gonads and five of them contained exclusively female gonads which could be identified as ovaries with well-developed yolk-filled eggs without a microscope. According to Okada & Miyashita the gonads of *Eriocheir* are normally of different sex. Thus these authors conclude that the observed parasitic intersexuality is analogous to the genetic intersexuality in insects (cf. p. 42) and can be explained in the light of the 'time-law'

for intersexual animals. Notwithstanding this opinion, the authors declare that real castration effects also occur in the complex 'parasitic castration', because Miyashita (1933) had earlier found a female of *Eriocheir* which was infected by a parasite belonging to the Entoniscidae, and in this female the abdomen persistently remained at a juvenile stage of development in spite of the considerable size of the animal, while the ovaries were very undeveloped. Okada & Miyashita (1935) concluded therefore that in this instance the growth of the abdomen was dependent on the development of the ovaries.

The complicated problem as to how manifestly female characters can be produced in male crabs which have been infested with Rhizocephala is not easy to solve. Koller (1937), who had no opportunity to take into consideration the work of Brinkmann (1936), finishes his critical review of this question in the following manner, laying special stress upon the fact, already hinted at by Brinkmann, that normally hermaphrodite gonads probably occur much more often in decapod Crustacea than was earlier supposed (for instance, in *Calocaris* and *Upogebia*). According to Koller, the starting-point of the changes which are caused by the parasite is a normal decapod Crustacean, genetically a male, but by hypothesis possessing the ability to produce ova in its testes. The parasitic infection decreases the male function of the testes and, instead, oocytes are developed. As a consequence certain hormones are produced which cause a development of the secondary sexual characters in a female direction.

The theory of the occurrence of sex hormones in Crustacea is favoured by some reliable experimental investigations of recent years. The experiments of Mori (1933), however, gave negative or almost negative results. After castration of male *Daphnia magna* with radium, no influence on the secondary sexual characters could be observed; in females the same castration prevents the development of the brood-pouch. This fact could not be attributed with certainty to the occurrence of sex hormones, since the radium treatment had partly injured the animals and therefore provided unfavourable experimental conditions. In papers by Haemmerli & Boveri (1926) and Le Roux & Legueux (1931, 1933) an evident connexion is nevertheless found between the degeneration of the ovaries after

radium treatment and the development of the secondary sexual characters.

According to Haemmerli & Boveri (1926) there exists in female *Asellus* a regular reproductive cycle (cf. Vandel, 1924), the chief phases of which are development of the ova, development of the brood-pouch, egg-laying, and taking care of the brood. Simultaneously with these phenomena regular moults occur when the brood-pouch is developed after copulation. In the treatment of ripe females the whole body was exposed to the action of radium, but a microscopical investigation showed that only the ovaries had been injured. Simultaneously with the degeneration of the ovaries the animals completely lost the power of producing a brood-pouch.

Similar results to those of Haemmerli & Boveri were reached by Le Roux & Legueux (1931, 1933) after radium treatment of female *Gammarus* (cf. Legueux, 1924, and Archangeli, 1932). In *Gammarus duebeni* the first stage of the development of the oostegites appears after the ninth moult. The oostegites grow until the thirteenth moult and are then supplied with bristles whose function is to keep the eggs in place in the brood-pouch, since yolk is first developed in the ova between the twelfth and the thirteenth moults. After the thirteenth moult the eggs are laid. If the animals are treated with radium before the appearance of the oostegites and then again before the appearance of the yolk, this substance is never produced and no bristles are developed on the oostegites. Radium treatment after egg-laying is followed at the next moult by the production of oostegites without bristles, and the egg-laying is inhibited. The treatment nevertheless does not destroy the ovaries but only retards their normal functional rhythm, for if the radium treatment is interrupted new oostegites with bristles are developed and egg-laying begins again. The development of the bristles must thus be causally connected with the development of yolk in the ova, when specific substances which act upon the oostegites are poured into the blood.

Finally, it may be mentioned that Sexton & Huxley (1921) trace back the cause of the development of intersexes in *Gammarus chevreuxi* to the reduction of the gonads, and Darby (1934, 1935) concludes from his investigations of intersexual forms and his regeneration experiments in *Uca pugilator* and *Crangon*

armillatus that sex hormones must be regarded as the cause of the different development of the claws in males and females of these two Crustaceans. According to Day (1935) in female *Carcinus maenas* there is also a correlation between the rate of growth of the abdomen and the beginning of sexual maturity: a correlation which does not necessarily depend upon but may be connected with a hormonal influence from the gonads. Finally, Edlén (1938) has found that the growth of the body as such (and the speed of growth) in *Daphnia magna* is so intimately connected with the development of the ovaries that it is necessary to assume that the growth is hormonally regulated by the ovaries. Though our knowledge in this respect is of course still very fragmentary, the hypothesis of the existence of sex hormones in Crustacea seems to be supported by evidence derived from many different investigations.

5. Insecta

Parasitic castration in insects has given rise to a literature even more extensive than that for Crustacea. Only a few papers can be specifically mentioned here. Of special interest in this connexion is the parasitic castration of aculeate Hymenoptera caused by Strepsiptera (cf. *inter alia*, Peréz, 1886; Perkins, 1892, 1918, 1919; Pierce, 1909, 1918; Wheeler, 1910; Smith & Hamm, 1914; Ulrich, 1927; Salt, 1927; Rabaud & Millot, 1927; Koller, 1929, 1937; Goldschmidt, 1931; Vandel, 1933). Among the Strepsiptera *Stylops melittae* lives in *Andrena cineraria* and other species, and *Xenos vesparum* in *Polistes gallicus*. The parasite is very large and encroaches upon all organs within the body-cavity, especially the gonads, and female hosts are completely castrated. The influence of *Xenos* upon *Polistes* can be traced in several respects, but an effect upon the development of the secondary sexual characters is not observed. In *Andrena*, on the other hand, not only are the secondary sexual characters changed through reduction, but a partial sex-reversal is brought about, male characters occurring in females and vice versa. The characters mostly involved in these changes are the apparatus for pollen-collecting in females, the form of the antennae, and the pattern of the clypeus.

Another pronounced instance of parasitic castration in insects has been described by Buchner (1925). It dealt with three

females of the cicada *Euacanthus*, the ovaries of which were completely reduced through the presence of a parasitic larva belonging to the Diptera. In *Euacanthus* there exist special organs, the mycetomes, which contain symbionts. The mycetomes of the females are provided with 'infection tubercles' from which the symbionts are transferred to the next generation. At the time of the maturation of the eggs, the symbionts show certain changes, and are transformed into infection forms which leave the mycetomes through the infection tubercles. In the males there are no infection tubercles and no infection forms of the symbionts. Now in the three castrated females of *Euacanthus* described by Buchner, the mycetomes were very well developed but the infection tubercles and the infection forms of the symbionts were absent. Buchner explains this fact on the supposition that in normal females 'specific female substances' are produced which act upon the development of the mycetomes and the symbionts.

In larvae of the cicada *Thelia maculata* the parasitic Hymenopteran *Aphelopus theliae* lays an egg which later gives rise through poly-embryony to hundreds of larvae, which feed upon the organs of the host and finally kill it (Kornhauser, 1919). Meanwhile, the gonads of the host are more or less injured, but in the testes of a male, the external characters of which were completely feminized, spermatogenesis was observed. In both sexes the copulatory apparatus is undeveloped, but, as in sacculinized Crustaceans, the males assume the female colour and form of the body and hairs.

Parasitic castration by nematode worms of the genus *Mermis* leads to the development of intercastes, intermediate forms between the normal castes, in social insects. The infected soldiers in ants especially show obvious signs of feminization, but though such intercastes are very common in animals infected by *Mermis* they are also found as a consequence of disturbed nutrition, and it is not necessary to postulate a hormonal influence in this instance. Buchner's interpretation of parasitic castration in *Euacanthus* has not been disputed, but on the subject of the other two instances of sexual changes in insects after parasitic castration (by Strepsiptera and by *Aphelopus*) and the sacculinization of decapod Crustaceans, Goldschmidt (1931) expresses the following opinion: 'In all three instances it is established that the degree of intersexuality is proportional to

the earliness of infection by the parasite. The time of onset of the action of the parasite is identical with the critical point in cases of zygotic intersexuality.'

It cannot be denied that the importance of the gonads for the development of the secondary sexual characters in insects, as revealed by experimental investigations, is nil or very slight. In this respect the insects not only differ from the vertebrates but also from the relatively very closely related Crustacea.

The first experiments on insect castration which were performed by Oudemanns (1897, 1899) in *Lymantria dispar*, a moth with striking sexual dimorphism, already showed that castration had no influence upon the development of the secondary sexual characters, such as form and colour of the wings and form of the body and antennae. Not only were physical qualities unchanged but also the behaviour; the males copulated without sperms, the females tried to lay eggs without ovaries, and so on. The same results were obtained by Kellog (1904, 1905) in *Bombyx mori*, and by Meisenheimer (1907–24) from elaborate and careful investigations on *Lymantria dispar*, *Lymantria monacha*, *Euproctis chrysorrhoea*, *Orgya gonostigma*, and *Gastropacha quercifolia*. Meisenheimer performed not only castrations but also transplantations, and was able to show that the transplanted testes thrived well in females and the ovaries in males, but they did not act upon the secondary sexual characters of the new owner. Original males which possessed no testes but transplanted and well-developed ovaries agreed completely in body-form, antennae, and colour of the wings with normal males. Organs which regenerated after the transplantation of the gonads of the opposite sex also showed no influence of the transplanted gonads, and the instincts remained unchanged. Kopec (1908–24) completed the experiments just reviewed in different species of Lepidoptera, using, besides castrations and transplantations of gonads, injections of extracts of the gonads and of blood from one sex to the other, and obtained the same results as Oudemanns, Kellog, and Meisenheimer. The same conclusions were drawn in principle by Regen (1909, 1910), who worked with *Gryllus campestris*, Prell (1914, 1915) after experiments with *Lasiocampa quercus* and *Cosmotriche potatoria*, Klatt (1919, 1920), investigating *Lymantria dispar*, and Geigy (1931), who castrated *Drosophila* by means of ultra-violet light and was

unable to find any evidence of sex hormones acting on the external sexual characters. Finally, Husain & Baweja (1936) have extirpated the gonads in *Schistocerca gregaria* and proved that the castrated animals live as long as normal ones, that they develop the yellow colour which distinguishes the normal sexually mature individuals, and that they copulate like normal animals.

Dewitz (1908, 1912), Steche (1912), and especially Geyer (1913) investigated the haemolymph in insects, which is different in males and females. These investigations gave the same results as those already mentioned. Neither castration nor transplantation nor blood transfusion affected this difference.

Some authors believe that the development of certain sexually dimorphic organs in insects is influenced by sex hormones. Thus Mercier (1920) thinks that spermiogenesis in Panorpids affects the development of the salivary glands, which are different in males and females; the maturation of the sperms stimulating and hastening the development of the glands in the males. Quignon (1926), too, is of the opinion that the growth of the horn in *Oryctes nasicornis* is due to a sex hormone. Facts which might be regarded with some probability as positive results of castration experiments are, however, very rare in insects. Thus Hamasaki (1932) found that castration in larvae of *Bombyx* is followed by a vigorous development of the fat-body and a retardation of metamorphosis, whereas Prell (1915) observed that the wing-colour in castrated and transplanted male *Cosmotriche potatoria* approached that of female animals. This approach to the female type should be obvious already in castrated males but much more so in castrated males which possessed a transplanted ovary. Meisenheimer, too, observed a wider range of variation of the wing-colour in operated animals, but Frings (1908, 1912) and Standfuss (1899, 1913) have shown that a marked lability of the colour dimorphism is especially characteristic of *Cosmotriche*.

These last-named observations by Prell, which, in other circumstances might have been regarded as strong arguments in favour of the hypothesis of the presence of sex hormones in insects, do not weigh much compared with all the negative results. Harms (1914, 1926), Lipschütz (1924), and von Buddenbrock (1928) have, however, pointed out that the

secondary sexual characters in insects might be influenced by an incretory organ which might not be located within the gonads and therefore would not have been injured during the castration experiments of Oudemanns, Kellog, Meisenheimer, and Kopec (cf. p. 72). Much the same conclusion was drawn by Spett (1930), who investigated the post-embryonic development of the secondary sexual characters in *Chorthippus parallelus*. These organs are but feebly developed during the younger stages, but reach their maximum as a result of a sudden spurt in their development. This makes Spett inclined to suspect an increased incretory activity, though this need not necessarily be due to the gonads.

IV

HORMONE-LIKE INFLUENCE ON THE GONADS FROM SURROUNDING ORGANS. INTRA-GONADIAL HORMONAL ACTION AND GENE HORMONES IN INSECTS

UNDER this heading I include several apparently different physiological phenomena, all of which nevertheless are probably of a hormonal nature, and perhaps all (except those described by Iwanoff & Mestscherskaja (1935)) will, in the future, be found to belong to the gene-hormone group of physiological processes.

During recent years several instances of structural or functional changes in the gonads themselves under the influence of the surrounding organs have been demonstrated in insects. Papers dealing with these phenomena include those by Dobzhansky (1931), who has investigated gynandromorphs of *Drosophila simulans*, Bytinski-Salz (1933), who studied hybrids in Lepidoptera, and Hadorn (1937), who has examined lethal mutants of *Drosophila melanogaster*. Bytinski & Salz transplanted ovaries of the pupae of an abnormal hybrid strain of Sphingidae into pupae of normal individuals. According to their genetical constitution the former should have interrupted their development during the pupal stage, but under the influence of the organs of the normal hosts the ovaries developed

normally. In a like manner Hadorn (1937) transplanted gonads of lethal mutants of *Drosophila melanogaster* to normal representatives of the species, and found that the ovaries, but not the testes, continued their development much longer than if they had remained within the body of the lethal form. Though not absolutely proved, it seems very probable that hormonal reactions are active in these processes.

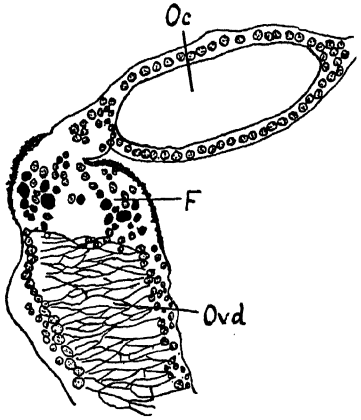


FIG. 5. Part of the ovary of a female *Blattella germanica* carrying an egg cocoon. *Oc* immature oocyte; *F* follicle which has released an egg and now contains yellow granules; *Ovd* oviduct. After Iwanoff & Mestscherskaja and Koller.

I have provisionally referred to the discovery by Iwanoff & Mestscherskaja (1935) of an incretory organ which in certain respects can be compared with the corpus luteum of mammals, as a case of intragonadial hormonal action. The term 'intragonadial hormone' is in so far correct that substances are produced from one portion of the ovary which act upon other portions of the same organ, but incorrect in so far as the substance may be (if it is not always) transported through the blood. The description by Iwanoff & Mestscherskaja of the different permeability of mature and immature ova in *Blatta orientalis* and *Blattella germanica* has already been briefly mentioned on p. 12. After maturation the ova are laid in cocoons which are carried for a considerable time at the genital opening of the female. During this period the ovaries (Fig. 5) again assume an infantile appearance, all growth-processes are inhibited, and the permeability of the egg-sheaths for stains is decreased to the same extent as found in larval ovaries. According to Iwanoff & Mestscherskaja the object of this retardation of the ovarian function is to prevent the passage of new ova through the oviduct, whose opening is closed by the egg cocoons. As soon as the cocoon is removed, oogenesis begins once more. That the retardation of the function of the ovaries is hormonally regu-

lated was shown by the authors by means of the following experiments. Iwanoff & Mestscherskaja transferred active ovaries to the body-cavity of a cocoon-carrying female, and within 30 to 60 minutes the transplanted ovaries showed the lower permeability which is characteristic of immature organs. The same authors showed further that the retardation-hormone is derived from the ovaries themselves; active ovaries which were put into extracts of inactive ones after a while assumed the lower permeability. It seems probable that the hormone is produced by the empty follicle which has just delivered the mature egg to the cocoon. In the protoplasm of the degenerated cells yellow or orange-yellow granules are produced which Iwanoff & Mestscherskaja compare with the contents of the corpus luteum in mammals (Fig. 5).

In the ovaries of mature queens of *Termes redemanni*, too, Ahrens (1935) has described a body which resembles the corpus luteum of mammals, but which thus far has been investigated only by histological and cytological methods. The cells in the distal portions of the ovarian tubes in close proximity to the degenerating follicle-remains of delivered mature eggs contain big, round, light-yellow pigment bodies which are not soluble in alcohol, chloroform, or xylol, are not identical with the lutein of mammals, and are not related to fats. On the contrary they show certain similarities to the yellow pigment which Hett (1933) has found in the connective tissue of the theca in vertebrates. Instead of the progressive development of the follicles as in higher vertebrates, a regressive development as in fishes and amphibians, is found in *Termes*.

The paper by Goldschmidt (1931; cf. Goldschmidt, 1938) on the transformation of the gonads of intersexual *Lymantria dispar* should be considered in this connexion. Goldschmidt studied the transformation of the ovaries into testes and vice versa, and found that the determining processes probably did not go on in the individual cells. On the contrary it was probable that the balance of the sex genes either stimulated the sheath of the ovary to produce a hormone acting upon the whole gonad in transforming it into a testis, or stimulated a group of cells at the point of attachment of the vas deferens to the testicular compartments to produce a hormone transforming the testis into an ovary.

Goldschmidt himself (1927, 1931) has pointed out that the manner in which the genes act upon the organism must be compared with a chemical activity (cf. Huxley, 1935), and is inclined to regard the active substances which are produced by the genes during this process as hormones (cell hormones of Koller, 1937), which as a rule are produced and act within one and the same cell. A series of investigations from the Kaiser Wilhelm-Institute in Berlin-Dahlem of recent years shows clearly however that the action of the gene hormones is not always limited within the boundaries of the cells, but that a certain gene in *Ephestia kühniella* can act through the blood upon organs which are situated far from the place of production of the active substance, i.e. in a way which must be regarded as truly hormonal. Papers dealing with this matter include those by Becker (1937), Caspari (1933, 1936), Plagge (1935, 1936, 1938), Kühn & Caspari & Plagge (1935), Kühn (1936, 1937), and Kühn & Plagge (1937).

In the flour moth, *Ephestia kühniella*, there are two different races, the wild form and a mutation, which differ in the following among other respects. In the wild race the imaginal eyes are black and the larval ocelli are strongly pigmented, the body of the larvae is reddish, and the testes are brownish-violet. In the mutant race the imaginal eyes are red and the larval eyes only feebly pigmented, whereas the body of the larvae and their testes are not pigmented. The more pronounced pigmentation of the wild race is due to the presence in the cells of the dominant gene A, against which the mutant possesses the recessive gene *a*. In ordinary circumstances these genes are supposed to act within the cells in which they are contained, but by means of transplantation Kühn and his co-operators have shown that the gene A in addition has a distance-action by means of the blood. Thus transplanted testes from a larva of the wild race are able to increase the pigmentation of the feebly pigmented host, which assumes darker skin, eyes, and testes. If such a larva of the mutant race, which contains transplanted testes from the wild race, pupates, the eyes of the imago do not show the original red colour, but are much darker, sometimes coffee-brown, or ranging from this to black. As transplanted ovaries and brains of the A-race act in the same manner (though more feebly; the effect of two ovaries is the same as that of one testis), the active

principle cannot be identified as a sex hormone. It must be produced by all organs whose cells contain the gene A.

It is of interest that the transplanted organ needs only a short time to exercise its influence upon the host. If transplanted A-testes are allowed to remain only three days in the larvae of the *a*-host, the imagines which are developed from these larvae receive dark eyes. The hormonal action is not limited to *Ephestia kühniella*. Transplanted egg-tubes of *Acidalia virgulata* had the same influence upon the pigmentation of the pupae of the mutated race as transplanted organs of the wild race. Finally, it has been shown that the hormonal action of the A-gene can also be traced in the second generation of pure *a*-animals; the pigment-activating hormones have thus been transferred from the mother to the offspring.

The investigation of the pigment-activating gene hormone has gone still farther. Thus Becker (1937) has extracted this substance with acetone from the body of the wild race, and after injection into *a*-animals the extract showed the same results as transplantation of A-organs. Similar extracts of *a*-animals, as also transplantation of *a*-organs to *a*-animals, had no influence upon the pigmentation. According to Becker the active principle is not a protein or lipoid-soluble substance.

In *Drosophila* there exist the same differences in the pigmentation between the wild form and a mutant race, and the pigmentation is influenced by a substance which is produced by the genes of the wild race. Thus simultaneously with A. Kühn and his co-operators, another team of scientists centred round G. W. Beadle and E. Ephrussi has made similar investigations on the gene hormone activity which regulates the pigmentation of the eyes in *Drosophila* (cf. the comprehensive papers of Beadle & Ephrussi, 1937, and Ephrussi & Beadle, 1937). During these investigations it was observed that extracts of the butterfly *Galleria* could replace the gene hormone of *Drosophila* which acts on the pigmentation of the eyes (Khouvine, Ephrussi, & Harnly, 1936), whereupon Becker (1937) made reciprocal injections between the different races of *Ephestia kühniella* and *Drosophila melanogaster*. These last experiments have made it probable, though still not completely certain, that the gene hormones which occur in the wild forms of these two species of insects and which act on the pigmentation of the eyes are identical.

V

INCRETORY ORGANS AND HORMONES CONNECTED WITH ECDYSIS, METAMORPHOSIS, AND REPRODUCTION IN INSECTS

I WILL first describe briefly the anatomy and histology of those organs in insects which are regarded as incretory, and later the hormonal reactions which with a greater or lesser degree of certainty are supposed to be derived from these organs.

1. Anatomy and Histology

A. **Corpora allata.** The embryonic development of the corpora allata was first described by Heymons (1895–9), who regarded these organs as a posterior pair of sympathetic ganglia connected with the innervation of the digestive canal. Later the anatomy, embryology, and histology of the corpora allata have been investigated by a number of scientists: Berlese (1908), Police (1910), Nabert (1913), Strindberg (1913), Holmgren (1909, 1916), Ilo (1918), Wiesmann (1926), de Lerma (1932, 1933, 1934, 1936), Wigglesworth (1934, 1935, 1936), Mellanby (1936), Graichen (1936), Burtt (1937), Pflugfelder (1937, 1938), Gerould (1938), and Schrader (1938). Of these works Nabert's constitutes an exhaustive review of the corpora allata in several representatives of all the more important insect groups, while Pflugfelder in three different papers in 1937 and one in 1938 has given a careful account of the corpora allata in the Hemiptera, Isoptera (*Termes redemanni*, *Microtermes amboinensis*), and Phasmida (*Dixippus morosus*).

According to Heymons and Nabert the corpora allata can be defined in the following manner. They take their origin from the ventral surface of the base of the maxillae as two invaginations which later extend in a dorsal direction and stop in the closest proximity to the oesophagus and the aorta. This description of the development has since been confirmed by Mellanby in the Hemiptera (*Rhodnius*) and by Wiesmann and Pflugfelder in the Phasmida (*Dixippus*). It is of special interest to note that Heymons (1899) is inclined to propose a homology

between the corpora allata and the maxillary glands in the Crustacea which serve as excretory organs (cf. also Holmgren, 1916).

The corpora allata can be paired or unpaired. They are unpaired in *Rhodnius* and other land Hemiptera according to Wigglesworth (1934) and Pflugfelder (1937); in *Ephestia kühniella* they are normally paired but sometimes fuse on the dorsal side of the oesophagus (Schrader, 1938). The corpora allata are situated in the neighbourhood of and behind the corpora cardiaca (pharyngea) and are commonly situated asymmetrically in the hind part of the head, in the neck, or in the foremost portion of the thorax (Plate III). They are mostly elongated sacs with thick walls and the following histological characteristics. They stain intensely with different stains, they contain osmophil secretion granules, and at least during certain stages of the secretory cycle vacuoles, the nuclei are rich in chromatin, and the gland seems to be of a syncytial structure. The corpora allata are surrounded by a thin sheath of connective tissue and are intimately connected with the aorta, whose wall at the boundary to the gland seems to be completely penetrable and is characterized by a special kind of cell (the 'Durchlasszellen' of Pflugfelder); cf. Plate I. 1.

Pflugfelder (1937) distinguishes in the corpora allata of *Dixippus* a cortex of elongated epithelial cells whose protoplasm contains vacuoles, and which surround an inner mass of secretory products. In the interior of this mass there are found some concentric structures which were earlier considered to correspond to the moults, an hypothesis which as regards the embryological origin of the corpora allata was not in any way improbable, but which according to Pflugfelder is incorrect. As to the innervation of the corpora allata, Pflugfelder has, both in the Hemiptera and in the Phasmida, found two pairs of nerves which together innervate these organs and the corpora cardiaca. In *Dixippus* these nerves leave the brain on the ventral surface of the protocerebrum. A medial pair of nerves innervates chiefly the corpora cardiaca, a lateral pair the corpora allata. Some nerve-fibres, however, enter the corpora allata from the corpora cardiaca. For the rest there is no consensus of opinion regarding the innervation of the corpora allata (which is certainly not quite uniform in different insects; cf. Nabert, 1913, and

de Lerma, 1936), but the presence of connexions with the sympathetic nervous system of the digestive canal, the ganglion hypocerebrale (ganglion oesophageum), seems to be a fact (Pflugfelder, 1937; de Lerma, 1936).

Police (1910) already regarded the corpora allata in the Phasmida as incretory organs, and Nabert (1913) extended this hypothesis to hold good for all insects; he also noticed a periodicity in their function. Later Wigglesworth (1935) has investigated this periodicity in *Rhodnius* in more detail and is inclined to connect it with the periodic moults. Pflugfelder (1937) observed in the Coccidae in which the corpora allata are paired, that these organs become rudimentary in the males after completed metamorphosis, whereas they continue to grow in the females and finally grow bigger than the brain. According to the same author the corpora allata in *Dixippus*, as in several other insects, show a functional cycle which can be cytologically defined. After each moult several mitoses are found, then follows a period of growth, and finally a period of very active secretion. The quantitative growth of the corpora allata in *Dixippus* follows that of the body itself, and when the body-weight is doubled after the last moult the corpora allata also show a considerable increase in volume.

Holmgren (1909) detected that the corpora allata in older termite queens undergo an enormous increase in volume and at the same time a change in structure. Holmgren believed this condition to represent a hypertrophic degeneration as a consequence of the abundant nutrition. Pflugfelder (1938) investigated the corpora allata in the different castes of *Termes redemanni* and *Microtermes amboinensis*. In these species the incretory organs are only slightly bigger in the queens than in the soldiers and workers until the time of the foundation of the colony. After the workers have developed and social activity has begun, the corpora allata of the queens rapidly increase in volume. The growth is due to the enormous growth of the cells themselves, since no mitoses occur in the organs. In particular the volume of the nuclei is increased from 40 to 50μ^3 to 400 (in *Microtermes amboinensis*), vacuoles are developed within the protoplasm, and secretory capillaries in the peripheral cells. The nuclei in the corpora allata of workers have a volume of 30 to 40μ^3 and do not show any considerable growth, whereas

in the soldiers the volume of the nuclei is doubled to 70–80μ^3 after the last moult.

As in the Coccidae, the corpora allata in Lepidoptera *Ephestia kühniella*) show a sexual dimorphism (Schrader, 1938). According to Yokoyama (1936) in *Bombyx* and Schrader (1938) in *Ephestia*, the corpora allata do not show any microscopically visible secretory activity during the larval stages, which fact is of importance from the point of view of the theory of the general function of these organs. In the larvae of *Ephestia* the nuclei of the large head-cells of the corpora allata are ellipsoid, but in the adults they have grown considerably and assumed a lobate form which is characteristic of secretory cells. This secretory nucleus is developed during the pupal stage simultaneously with the appearance of different secretory products in the protoplasm. Mitoses do not occur during the pupal stage. According to Schrader connective-tissue nuclei are found in the interior of the corpora allata in the imago of *Ephestia*, as well as some tracheoles and a number of vacuoles which increase with age. The number of cells in the corpora allata is the same in males and females of the imagines in *Ephestia*, but, contrary to the case in the Coccidae, in *Ephestia* the cells of the males are much bigger than those of the females, and thus the male corpora allata of *Ephestia* grow much bigger than the female. The secretory products and the nucleoles in the corpora allata are also dissimilarly developed in male and female *Ephestia*.

Whereas, according to Burtt (1937) and other authors, the corpora allata in the larvae of *Chironomus* and *Tipula* seem to have the same structure and form as in most insects, the same organs in the larvae of such Diptera as the blow-fly, *Calliphora*, according to Burtt and Hadorn (1937), have assumed the form of 'Weissman's ring'. In *Calliphora vomitoria* this 'ring' (Fig. 6) is situated on the dorsal side of the cerebral lobes and surrounds the aorta, which is attached to it dorsally and ventrally but laterally is free (Burtt, 1937). The organ is invested with a fine connective-tissue coat continuous with that of the aorta, and contains the following cell-types: (1) a group of small darkly staining imaginal cells with little cytoplasm which are situated around the tracheae which traverse the ring; (2) a few cells of nervous type scattered through the ventrolateral portion of the ring; and (3) large cells with large nuclei, rather indistinct

cell-boundaries, and often showing vacuoles in the cytoplasm. These are the secretory cells. Burtt believes these structures to be the modified and fused corpora allata, an opinion which needs confirmation by further investigation. By comparison in particular with the paper of Pflugfelder (1937) on the corpora allata

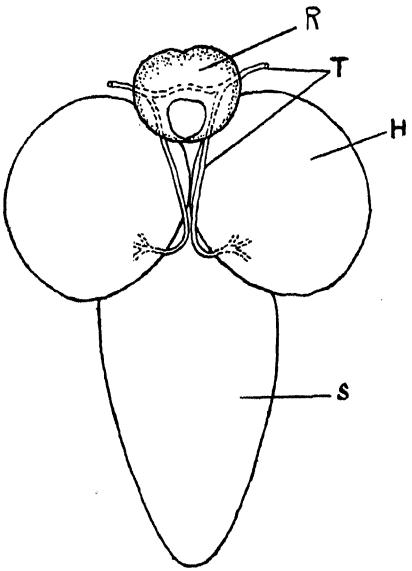


FIG. 6. Situation of the ring gland of a *Drosophila* larva in respect of the central nervous system (semi-schematic). *R* ring gland; *T* tracheae; *H* hemisphere; *S* sub-oesophageal ganglion. After Hadorn.

in *Dixippus morosus*, it seems to me more probable that the structures described by Burtt (1937) represent a stage in the ontogenetic development of the corpora cardiaca. This theory is favoured by the fact that nerve-cells are said to be found in the ring-gland and also occur in the corpora cardiaca (p. 55), whereas the corpora allata do not contain any nervous elements.

B. **Corpora cardiaca.** The corpora cardiaca (Berlese, 1908; Holmgren, 1909; Nabert, 1913; de Lerma, 1933, 1936; Baden, 1936; Pflugfelder, 1937; cf. also Hanström, 1928) have in the past most often been regarded as sympathetic ganglia (pharyngeal ganglia, lateral sympathetic ganglia, corpora pharyngei, corpi faringei), and are developed as an invagination from the

stomodaeum in the neighbourhood of the ganglion hypocerebrale (ganglion oesophageum). After completed metamorphosis they are situated between the brain and the corpora allata (Plate III). They finally join the wall of the aorta so intimately that they seem to represent an integral portion of it (Plate I. 2). According to Pflugfelder (1937) they contain two

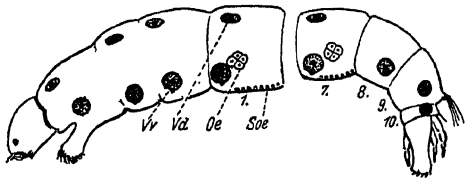


FIG. 7. *Syndiamesa branicki.* Segmental arrangement of the ventral (*Vv*) and dorsal (*Vd*) Verson glands and the oenocytes (*Oe*) in a mature female larva. *Soe* Synoenocytes. 1–10 abdominal segments. After Zavrel.

cell-types; nerve-cells and osmophil cells, which later possess a secretory or excretory function. The innervation of the corpora cardiaca is described on p. 51. A functional cycle has not been proved to exist in the corpora cardiaca, but they increase considerably in volume in older sexual individuals of termites (Holmgren, 1909; Pflugfelder, 1938).

C. **Oenocytes, Synoenocytes, and Verson Glands.** Wielowiejski (1886) and Verson (1890) first distinguished three different kinds of epithelial glands in Chironomidae and *Bombyx mori.* These were called by Zavrel (1935) oenocytes, synoenocytes, and Verson glands. The oenocytes were given their name by Wielowiejski on account of their wine-yellow colour in the Chironomidae which is probably derived from a chromolipoid. There exists an extensive literature on the oenocytes (among others Verson, 1900, 1911; Rössig, 1904; Weissenberg, 1906; Stendell, 1911, 1912; Kreuscher, 1922, 1923; Poison, 1924; Koller, 1929; Rösch, 1930; Albro, 1930; Weber, 1933; Wigglesworth, 1934; Mellanby, 1936; and Zavrel, 1935, 1938).

The oenocytes (Figs. 7, 8) are usually composed of a few cells which are formed from the embryonic epidermis in the neighbourhood of the abdominal stigmata through enlargement of isolated epithelial cells or from subepidermal cells which have

already lost their continuity with the epidermis. The oenocytes later either remain in an intimate connexion with the epithelium and are segmentally arranged, or move farther inwards and are distributed among the cells of the fat-body (corpus adiposum). Their cells are comparatively large and round and stain intensely; the protoplasm contains secretory capillaries and vacuoles.

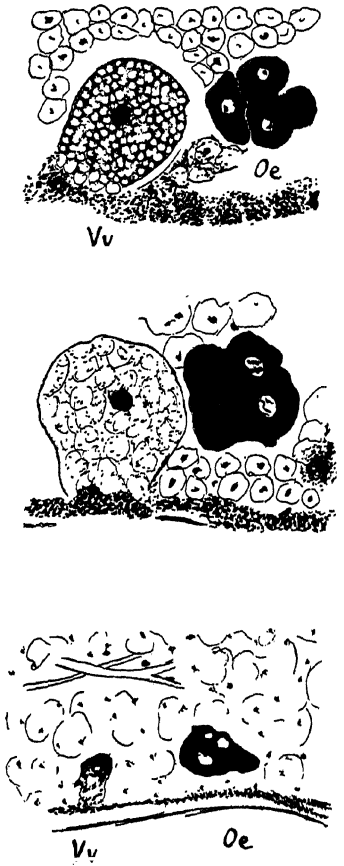


FIG. 8. Three successive functional stages of the ventral Verson glands (*Vv*) and oenocytes (*Oe*) in *Syndiamesa branicki*. In the lowest row, hatching pupa. Schematically after Zavrel.

Zavrel (1935, 1938) distinguishes oenocytes (or larval oenocytes) and synoenocytes. At the very moment when the last larval skin is ready to be shed, the oenocytes and the Verson glands in the Chironomidae reach their highest development and are filled with vacuoles. When the old skin is cast, the oenocytes shrink, degenerate, and disappear. They now are replaced by the synoenocytes, which appear for the first time just before the last larval moult in the larva prepared for pupating. Zavrel has found functional cyclic changes in the oenocytes and the Verson glands of the larvae, and in the synoenocytes of the imagines.

In the Chironomidae the synoenocytes show a certain sexual dimorphism. The larvae of the last stage possess synoenocytes only in the pregenital abdominal segments, that is, 1–7 in the females and 1–8 in the males. In the females they are larger and show a retarded development (Zavrel, 1938).

The Verson glands (Verson, 1890, 1892, 1902, 1911; Anglas, 1901; Schulze, 1912; von Buddenbrock, 1930; Hoop, 1933; Weber, 1933; Wigglesworth, 1934; Zavrel, 1935, 1938; Schürfeld, 1935; Koller 1937) occur in the Lepidoptera (*Bombyx mori*) in a segmental arrangement (Figs. 7–9), mostly fifteen pairs in the thorax and the abdomen. In the Chironomidae (*Syndiamesa branicki* according to Zavrel) there exist both dorsal and ventral Verson glands in all three thoracic segments and the first seven abdominal segments, whereas the abdominal segments 8–10 each possess only one Verson gland.

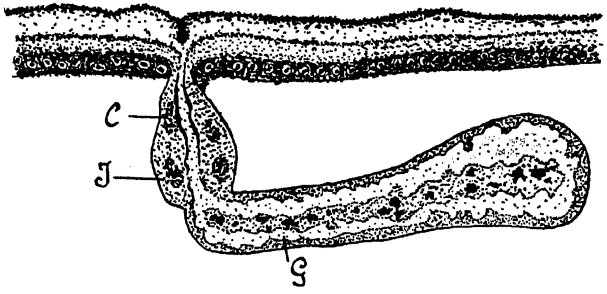


FIG. 9. Verson gland, semi-schematic. *C* canal cell; *I* intercalary cell; *G* gland-cell. Simplified after Schürfeld.

Each Verson gland contains three cells: the canal cell, the intercalary cell, and the gland-cell (Fig. 9). Anglas (1901) already was inclined to regard the large gland-cell of the Verson organs as an incretory one whose function was connected with moulting, but the common opinion has been that it produced the fluid (the exuvial fluid) which is secreted at the moults between the old and the new cuticle. In agreement with Schulze, von Buddenbrock also regarded the canal cell and the intercalary cell as secretory, considering that the opening of the canal was situated on the outer side of the cuticle and that the gland-cell was not connected with the canal. According to von Buddenbrock, the gland-cell was therefore an incretory organ connected with pupation, and the two exterior cells were not able to produce the exuvial fluid because they opened out on the surface of the cuticle. The anatomical and physiological investigations of Schürfeld (1935) in *Smerinthus ocellata* have, however, proved that the large secretory cell of the Verson glands is really

connected with the canal which is surrounded by the canal cell and the intercalary cell, and that this canal opens out between the old and new cuticle (Fig. 9). The Verson glands are therefore in fact the exuvial glands.

D. **Corpus adiposum (the fat-body).** The fat-bodies, or the corpus adiposum (Plates I and III), are derived from the ventral walls of the coelomic sacs and are therefore originally arranged segmentally. Later, the different portions join to form a visceral and a parietal layer (Schmieder, 1928; Weber, 1933). During certain stages of their functional activity the cells of the fat-bodies form a syncytium; especially in holometabolous insects they show vital changes during metamorphosis, they contain besides fat-droplets also glycogen and proteins, and possess an irregularly formed nucleus. This form of the nucleus is certainly connected with the intense metabolism of the cells, which is supposed to be associated with the synthesis of vital substances of the body (Weber, 1933).

A new and extensive study of the fat-body in *Simulium* has been published by Scriban & Dragut (1935). The inner fat-body consists of two strings which are branched at certain intervals. In their hindmost portion they join and surround the digestive canal and the central nervous system and almost fill the body-cavity. The outer fat-body forms a layer of fat beneath the dorsal and lateral integument. Besides fat-droplets it contains yellow pigment-granules which show typical melanin reactions.

2. Hormonal Regulation of Metamorphosis in Insects and its Connexion with the Brain, the Corpora allata, or other Incretory Organs

The hormonal reactions which are connected with the metamorphosis of insects have recently been comprehensively treated by Bodenstein (1936), Hase (1936), and Koller (1937). The first to discover the possibility of a hormonal regulation of insect metamorphosis was Kopec (1922), who proved that if larvae of *Lymantria* were deprived of their brain at an early stage of the development no pupation took place, whereas extirpation of the brain during later stages did not prevent the process of pupation. Kopec believed, therefore, that during an early stage of development a stimulus for pupation must emanate from the

brain, which stimulus probably belonged to the class of hormonal reactions. It is not easy to explain the integrated regulatory mechanism that releases simultaneously all those processes which are connected with the moulting and pupation of insects. Another possibility would be to suppose that all cells of the larval body have the same rate of development; yet another that the mechanism is regulated by means of the nervous system. The hypothesis of a nervous regulation would certainly cover the many instinctive reactions which occur at the time of moulting and pupation, but does not explain the simultaneous processes in the skin, the tracheal system, and the ectodermal portions of the digestive canal which occur at the time of moulting because these organs are, to a large extent, not innervated. Several transplantation experiments by Bodenstein (1932–6), Furukawa (1935), and Mauser (1935, 1937) can be cited against the hypothesis that all cells in the larval body have the same rate of development.

Bodenstein investigated *Vanessa urticae* and *Vanessa io*, obtaining the following results. If a larval leg from the fourth stage is transplanted to an older larva of the same stage it moults simultaneously with the host, i.e. earlier than normally. Transplantation between different species gives the same result. If a leg of a larva which has moulted for the last (fourth) time is transplanted to a larva which is just preparing for this moult, the leg moults again simultaneously with the host, i.e. performs an additional fifth moult without producing a pupal leg. The results of these experiments can hardly be explained without the hypothesis of hormones circulating in the blood.

In agreement with the experiments by Bodenstein, Furukawa (1935) was able to induce an additional and superfluous moult in imaginal portions of the antennae in *Anisolabis maritima* which were transplanted in place of cerci to young larvae of the same species, and Mauser (1935–7) obtained practically the same results in *Dixippus morosus*. In this species there occurs at the base of the inner side of the first leg of female imagines a bright-red spot. If this first leg is transplanted from older larvae to younger or from younger to older, the transplants moult simultaneously with the host and the red spot does not occur before the host has moulted into the imaginal stage. Transplanted

imaginal fore-legs also moult synchronously with the host if they are transplanted to younger stages, but retain the red spot.

Von Buddenbrock (1928, 1930) and Koller (1929; cf. Koller, 1937) tried to prove the existence of hormones regulating metamorphosis by blood-transfusion. Blood from animals preparing to moult in *Sphinx ligustri* was injected into larvae of the same species, after which an earlier moulting was sometimes observed. In a number of instances it was also possible to cause last-stage larvae of *Dilina tiliae* still consuming food to pupate earlier after injection of body-fluid from animals just preparing to pupate. Schürfeld (1935) repeated the experiments of von Buddenbrock extensively on *Smerinthus ocellata*, and after statistical revision reached the following conclusion: 'The final results of five series with 609 statistically useful animals do not permit the statement that the injection of "pupation blood" into larvae not prepared for pupation promotes pupation. Thus it is impossible to prove in this manner the existence of a pupation hormone which shortens the time between moulting and pupation.' Schürfeld also says that simply pricking the animals without injection of blood can cause an earlier pupation.

The metamorphosis hormones in insects (there are probably more than one) are classified by Bodenstein (1936) as larval, which cause the moults from one larval stage into another; pupation hormones, which cause the oldest larvae to pupate; and imaginal, which in hemimetabolous insects cause the last-stage larvae to metamorphose into imagines (Koller's 'Umwandlungshormon') and in holometabolous insects cause the pupa to develop into an imago. The pupation hormones of course are only found in holometabolous insects (Koller's 'Verpuppungshormon').

Of fundamental importance for our knowledge of the hormonal processes which cause moulting in the larvae are the experiments by Wigglesworth (1934–6), in which the blood-sucking hemipteran *Rhodnius prolixus* was investigated. *Rhodnius* has five nymph-stages, and during each of them the larva feeds only once, after which an almost exactly definite period elapses before the next moult. Wigglesworth decapitated larvae at different times after the feeding, and found that decapitation before the third to fifth day after feeding prevents moulting, but decapitation after this critical period does not. Within the head of *Rhodnius* a factor must thus exist without which moulting cannot take

place, and this factor is found in the blood before the third day after feeding. If two nymphs are decapitated, one before, the other after, the critical period, and these nymphs are joined by the ingenious method used by Wigglesworth, both undergo a moult. The older larva is thus able to induce moulting in the younger, though the latter is not itself able to do so. Blood transfusion from an older to a younger larva can also cause the latter to moult. The action of the moult-stimulating hormone is not limited to the species, for reciprocal joinings between *Rhodnius* and *Triatoma* gave the same result (Plate II. 3).

FIG. 10. Constriction experiments in *Calliphora erythrocephala*. A. The body was constricted after the critical period and both the anterior and the posterior portions of the body pupated. B. The body was constricted before the critical period and only the anterior portion of the body pupated. Simplified by Koller after photos by Fraenkel.

According to Wigglesworth, 'some rather indirect experimental evidence is given that the corpus allatum secretes the moulting hormone'.

By means of constriction experiments in insect larvae preparing to pupate (the Diptera *Calliphora erythrocephala* and *Drosophila melanogaster* and the Lepidoptera *Lymantria dispar*, *Ephestia kühniella*, *Sphinx ligustri*, *Deilephila euphorbiae*, and *Bombyx mori*), Kopec (1922), Fraenkel (1934, 1935), Caspari & Plagge (1935), Bodenstein (1936), Bounhiol (1936), Kühn & Piepho (1936), and Bodenstein (1938), proved that only those parts of the larvae which contain the brain region pupate if the operation is done during a certain early larval stage (Fig. 10). If the operation is done later the posterior parts of the larvae also pupate. The pupation of the hind portions in the last-named case takes place also if the nervous connexion between the fore- and hind-parts of the body is interrupted (Fraenkel, 1935). These facts are in favour of the existence of an incretory organ in the anterior part of the body, and according to certain experiments either the brain itself (Kopec, 1922; cf. also Tirelli, 1924), or an

organ which is situated in closest proximity to the brain, secretes the active substance. As in the common larval moultings so in the activity of the pupation hormone a critical period is observed. If the brain is extirpated before this period in larvae of *Sphinx* and *Deilephila* they never pupate, though they can be kept alive for 35 days after the operation (Caspari & Plagge, 1935). Extirpation of the brain after the end of the critical period does not prevent pupation. Finally, if brains are transplanted to larvae which have lost their brains before the critical period, pupation can be induced in 50 per cent. of the animals investigated.

Kühn & Piepho (1936) believe that the brain itself or an organ in close proximity to it produces the pupation hormone. Now it is a fact that the corpora cardiaca are commonly situated nearer to the brain than the corpora allata (Plate III), but the cyclic changes in the last-named incretory organs (already observed by Nabert, 1913) were regarded as a sign that the corpora allata secreted the moulting and pupation hormones. For a long time the corpora cardiaca were regarded as representing purely nervous and not incretory organs, an attitude which may have contributed to the opinion that the corpora allata alone are functionally connected with metamorphosis. Besides the investigations by Wigglesworth, already mentioned on p. 60, a few authors have in recent years tried to investigate this problem. Thus Bounhiol (1936) extirpated the corpora allata in *Bombyx mori*, and was not able to find any influence on the time of pupation, which took place in a normal manner. This result was confirmed by Plagge (1938) in other Lepidoptera (*Deilephila elpenor*, *Sphinx ligustri*, and *Sphinx pinastri*, but especially in *Deilephila euphorbiae*).

By means of a new technique Plagge (1938) was able to confirm the presence of a pupation hormone in the Lepidoptera by blood transfusion. The critical period of the commencement of pupation in *Deilephila euphorbiae* is distinguished by the appearance of the burrowing instinct. Simultaneously with this begins the secretion of the pupation hormone, whose action can be prevented by constriction of the anterior part of the body or by extirpation of the brain before the beginning of the critical period. Larvae in which the brain was extirpated before the critical period could be caused to pupate after transplantation

of a brain or after transfusion of blood from a larva preparing to pupate. During these experiments the same result was obtained if the brain alone or the brain together with the corpora allata were transplanted. Thus the statements of Bounhiol were confirmed: these results also are in agreement with Schrader's (1938) histological observations according to which the corpora allata in *Ephestia kühniella* do not show any secretory activity before the pupa stage.

Still another investigation of the pupation hormone in *Ephestia kühniella* should be mentioned in this connexion, namely that of Kühn & Piepho (1938). This deals with the reaction of the hypodermis and the Verson glands to the secretion of the pupation hormone into the blood. The transformation of the larva into a 'primary pupa' ('Vorpuppe') in *Ephestia* is distinguished by the loosening of the larval eyes from the hypodermis, and simultaneously the critical period begins, during which the pupation hormone is secreted from the brain into the blood, as was proved by constriction experiments and extirpation of the brain. When the larva has ceased to move, a period of mitosis begins within the hypodermis, starting at the anterior end and continuing backwards. During the period of mitosis the hypodermis is separated from the larval cuticle, beneath which exuvial fluid is secreted. Then the development of the new cuticle begins, whereas the old is dissolved except for the outer, limiting membrane. The same processes take place in the tracheal system simultaneously with those in the skin. Constriction before the critical period prevents the commencement of the mitosis period and all other changes which accompany the pupation in that part of the body which is constricted from the brain. The Verson glands produce their secretion during the critical period, and immediately before or during the moult into the pupa, the fluid is poured out through a canal (Fig. 9) which is developed within the intercalary and canal cells (p. 57). The constriction of the fore-body from the hind-body also prevents the secretion of the Verson glands behind the ligature; they thus do not constitute incretory organs but themselves react to the pupation hormone derived from the brain. At a certain point of reaction of the hypodermis to the activity of the pupation hormone, the secretory activity of the Verson glands starts. The first-mentioned exuvial fluid, which is secreted into

the space beneath the old cuticle and according to Kühn & Piepho dissolves it, is derived from the hypodermis cells. This secretion starts before the activity of the Verson glands has begun.

The investigation of Schrader (1938), which was made in co-operation with Kühn & Piepho, completes the work of the latter in the following respects. If a brain from a larva of the fifth stage is transplanted to a full-grown larva, the regenerated hypodermis above the transplant (and parts of the adjacent hypodermis) at the next moult (the pupation moult) produces a larval cuticle; the rest of the hypodermis produces pupal cuticle, these two being structurally different. Thus the transplanted brain, which is younger than the host, must produce a substance which causes the hypodermis to produce larval instead of pupal cuticle. In spite of the concordant results, which prove that the brain itself in the Lepidoptera serves as an incretory organ, Schrader was not able to detect any cells within it which showed signs of an incretory activity. This is still more remarkable since neuro-secretory cells are found in the brain of several invertebrates, also in insects (cf. p. 140).

Whereas the experiments which have just been reviewed support the theory that in Lepidoptera the brain itself and not the corpora allata (or corpora cardiaca) secretes the pupation hormone (and according to the above-mentioned observation of Schrader also the larval moulting hormone), it seems equally evident that a special incretory organ within the head produces the pupation hormone in the Diptera. Weissman (1864) and Lowne (1890–5) described in *Calliphora vomitoria* a ring gland which surrounds the aorta and is situated in front of the brain hemispheres. Hadorn (1937) has found this organ again in *Drosophila melanogaster* (Fig. 6) and was able to show that it hastened the onset of pupation (cf. p. 53). Thus larvae of the lethal mutant race 'lgl' are able to pupate, but do so considerably later than normal larvae. Transplantation of ring glands of normal *Drosophila* to the lethal larvae accelerated pupation, whereas transplanted brains had no influence in this respect. Hadorn further transplanted ring glands of normal larvae, prepared for pupation, to younger normal larvae, and was thus able to accelerate the time of pupation in these. If three ring glands were transplanted to the same larva, the action was

stronger than if only one was transferred; the glands, however, only promoted the development of the puparium, and not that of the imaginal disks. The action is not specific, because a ring gland of *Drosophila melanogaster* acts upon the pupation in *Drosophila hydei*, which normally has a slower development than the former, and ring glands of *Lucilia* are active in *Drosophila melanogaster*.

Hadorn points out that there are certain resemblances between the ring gland and the corpora allata (cf. p. 54), though an embryological study would be necessary to decide whether the two organs are homologous. As I have already emphasized, it seems more probable that the ring gland is homologous with the corpora cardiaca, especially on account of its intimate connexions with the aorta. Though Burtt (1937), who has investigated the ring gland in *Calliphora vomitoria*, is also inclined to compare it with the corpora allata, it seems to me that his description and figures are more reminiscent of the corpora cardiaca. Fresh anatomical and embryological investigations are necessary in this field.

In this connexion the investigation by Steopoe & Dornesco (1936) of the changes in the neurilemma of the ganglia in *Bombyx mori* during the pupal stage may be mentioned. The simple single-rowed perineurium of the older larvae is exchanged in the pupa for large polygonal cells, but during the last days of metamorphosis these again disappear, and a single-rowed perineurium of flat cells is formed. In the hypertrophy of the perineural cells during the pupal stage Steopoe & Dornesco believe they have found a sign of an endocrine function connected with the histolysis and the histogenesis.

Because the hemimetabolous insects do not have a pupal stage it might be expected that the last moult before the imaginal stage would be regulated by the same moulting hormone as the earlier larval moults. It is possible that this is the case, but some observations of Wigglesworth (1934–6) are in favour of the hypothesis of the occurrence of different moulting and 'metamorphosis' hormones ('Umwandlungshormon' of Koller, 1937; inhibitory hormone of Wigglesworth) in *Rhodnius*. Thus Koller writes: 'Es ist sehr leicht möglich, dass zwischen Häutungs-, Verpuppungs- und Umwandlungshormon sehr nahe Beziehungen in chemischer Hinsicht oder auch bezüglich ihrer

Bildungsweise bestehen. Solange uns die Hormone nur in ihren verschiedenen physiologischen Wirkungen bekannt sind, müssen wir sie — bevor das Gegenteil nachgewiesen ist — als verschiedene Hormone betrachten.'

In *Rhodnius prolixus* (cf. p. 60) the nymph of the fifth stage is developed into the imago. During this metamorphosis there exists a critical period 6–8 days after the feeding (the feeding in this blood-sucking insect takes place only once during each larval stage). Decapitation of the nymph during the first days before the critical period prevents the 'metamorphosis' (the last moult into the imaginal stage), but decapitation after the end of the critical period has no influence; the metamorphosis takes place in a normal manner. The special form of the head of *Rhodnius*, with the long neck, makes certain instructive operations possible (Plate II). If a fifth-stage nymph is decapitated after the critical period and joined to a fourth-stage nymph which was decapitated before the critical period, this latter nymph will undergo a precocious metamorphosis and develop adult characters. A joining of a fifth-stage nymph preparing for the metamorphosis moult with a small first-stage nymph also causes an incomplete metamorphosis, and gives rise to a dwarf imago (Fig. 11). Wigglesworth also tried the opposite experiment. If a fifth-stage nymph is decapitated before the critical period and joined to a fourth-stage nymph in which the brain and the corpus allatum (unpaired in *Rhodnius*) remain, an additional moult is induced, which gives rise to a giant nymph. In these experiments the active substance is produced by the corpus allatum. Thus fifth-stage nymphs with the corpus allatum of third- or fourth-stage nymphs implanted in them give rise to 'sixth-stage' nymphs, and these 'sixth-stage' nymphs may give rise to 'seventh-stage' nymphs when they moult again.

The above experiments, which proved that in *Rhodnius* a difference must exist between a factor causing the common larval moult and another causing the last metamorphosis moult, were completed by other experiments. These made a more complicated hypothesis necessary than the simple supposition that a moulting hormone occurs during the nymph stages and a metamorphosis hormone at the transformation of the nymph into the imago. Thus if series of fourth-, third-, second-, or first-stage nymphs are decapitated around the critical period without

joining with other animals, some of them show more or less complete metamorphosis; others are intermediate between nymphs and adults. Thus according to Wigglesworth the moulting hormone is secreted at the beginning of each critical period, but its action is suppressed by an inhibitory hormone which

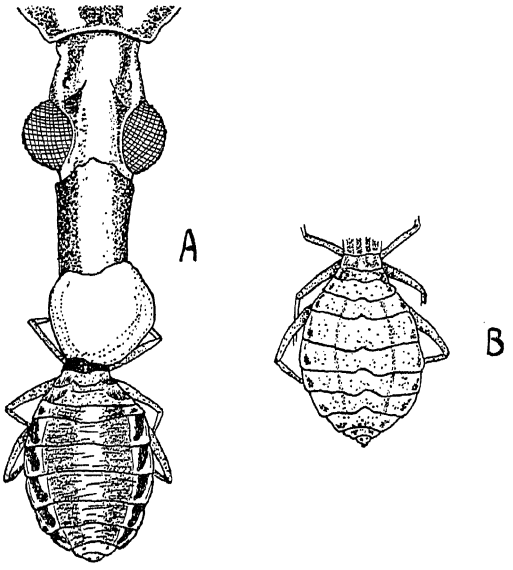


FIG. 11. A. Precocious 'adult' of *Rhodnius prolixus* produced from a first-stage nymph by joining it to a head of a moulting fifth-stage nymph. B. Normal second-stage nymph for comparison. After Wigglesworth.

seems to be secreted after the moulting hormone. This inhibitory hormone prevents metamorphosis in the earlier nymphal stages, but is secreted in such small quantities—or not at all—during the last moult that the metamorphosis takes place.

Wigglesworth himself has emphasized that it is not necessary to suppose that the moulting hormone and the inhibitory hormone are chemically different. The different actions might be connected with a different concentration of the same substance during different stages of development. Koller (1937) lays stress upon the following possibilities:

1. Only one kind of metamorphosis hormone exists in *Rhodnius*,

which, according to its different concentrations in the blood, has different actions.

2. There exist one moulting and one inhibitory hormone. Together they cause moulting, but moulting hormone without inhibitory hormone causes metamorphosis.
3. There exist three hormones—moulting, metamorphosis, and inhibitory hormone. The moulting hormone induces larval moults, whereas the metamorphosis hormone and the inhibitory hormone neutralize one another. At the last moult, which results in the imago, probably only the metamorphosis hormone is active—at least no inhibitory hormone is present.

Wigglesworth (1936) was also able to show that the effect of both the moulting and the inhibitory hormone is non-specific, since moulting hormone from *Rhodnius* will induce moulting in bugs of the allied genus *Triatoma* (Plate II. 3) and in the bed-bug *Cimex* after the joining of the animals in the manner described earlier. The same is true regarding the inhibitory hormone, as was proved through experiments with *Rhodnius*, *Triatoma*, and *Cimex*.

Hormonal processes may also be active at the transformation of the pupa into the imago in holometabolous insects. According to Hachlow (1931) and Bodenstein (1936), in these instances the activity emanates from the anterior part of the body in which Hachlow localized the active centre in the ventral portion of the thorax. Bodenstein (1938) continued these investigations in *Drosophila melanogaster*, and proved that in the anterior part of the thorax a centre exists the activity of which starts twenty-four to forty-eight hours after pupation. Extirpation of the anterior end of the pupa, including the centre, before this critical period prevents the development of the imaginal ectoderm; but if the same portion of the pupa is extirpated later, the ectoderm shows a normal development. The development of the imaginal disk for the compound eyes is also dependent upon the activity centre in the thorax, as combined constriction and transplantation experiments proved. The existence of an activity centre for the development of the imaginal ectoderm in the pupal thorax was confirmed by Bodenstein (1938) also in the moth *Phryganidia californica*. Various experiments seemed, however, to make it probable that

the impulse for the development of the imaginal ectoderm (which proceeds from the activity centre forwards and backwards) was not conducted by means of the blood but along the ectoderm itself. Bodenstein finally points out that the pupal activity centre in the thorax evidently does not act upon the development of all organs of the body, and proved that the development of the ovaries, for instance, is independent of this centre. Further investigations of hormonal influence upon metamorphosis in insects are reviewed on p. 73.

3. The Function of the Corpora allata, Corpora cardiaca, the Oenocytes, Synoenocytes, and Corpus adiposum

According to Wigglesworth (1934, 1936) there is some experimental evidence that the corpus allatum in *Rhodnius* (Hemiptera) secretes the moulting hormone, whereas it seems to be a fact that the inhibitory hormone which prevents metamorphosis in earlier stages is really produced by the same organ. Pflugfelder (1937), too, has found a certain influence of the corpora allata on moulting in the Phasmida (*Dixippus morosus*). *Dixippus* has six nymph-stages; then follows the last moult, the 'metamorphosis moult', which results in the imago. If the corpora allata are extirpated during the fifth and sixth nymph-stages, no influence upon the development is observed. If, instead, they are extirpated during the third and fourth nymph-stages, the animals moult only twice and then become sexually mature. These experiments show that the corpora allata in *Dixippus* are able to produce a quantity of moulting hormone during their presence in the body sufficient for two further moults; later the store of the hormone is consumed. The same experiments also make it probable that the presence of the moulting hormone alone is not sufficient to induce moulting, because according to the result of the investigation after each moult the body must have a sufficient store of the hormone to cause an immediate further moult. Either the tissues of the body must possess a certain maturity in order to moult, or the presence of an inhibitory factor must be postulated.

The fact that, according to Pflugfelder (1937), the corpora allata in *Dixippus* still continue to grow after the last moult supports the hypothesis that they possess another function besides the production of the moulting hormone. Now in the

males of the Coccidae these organs are rudimentary after completed metamorphosis, whereas in the females they continue to increase considerably in volume. Because female Coccidae, contrary to males, continue to feed after accomplished metamorphosis, and because the corpora allata in the queens of termites increase enormously in volume and function, Pflugfelder suggests that the corpora allata are also concerned in the regulation of the metabolism of the body. This would, further, be confirmed by the fact that the corpus adiposum in *Dixippus* shows a curious degeneration after the extirpation of the corpora allata.

Wigglesworth (1936) has found still another hormonal function connected with the corpus allatum in *Rhodnius* (Plate II. 4–8). According to the results of his extirpation experiments, the corpus allatum in the adult female is necessary for the production of mature eggs. In the absence of this secretion the oocytes continue to grow as long as they are connected to the nurse-cells, but die and are absorbed when their nutrition is taken over by the follicular cells. The corpus allatum is also necessary for the normal activity of the accessory glands in the adult male. The secretion of the male corpus allatum will induce egg development in the female, and the secretion from the female activates the accessory glands in the male. This sex hormone from the corpus allatum is non-specific, since the secretion from the corpus allatum of *Triatoma* will cause egg development in *Rhodnius* (Plate II. 5). But the sex hormone seems not to be the same as the moulting hormone of the nymphal stages, since this will not cause egg development in the adult female, and the egg-forming hormone does not induce moulting.

The investigations of Weed (1936) on the influence of an extirpation of the corpora allata in the Orthoptera Saltatoria (*Melanoplus differentialis*) are in considerable agreement with Wigglesworth's results. If these organs are extirpated nine days after the last larval moult, the metamorphosis moult takes place in a normal manner but the development of the eggs is delayed. In *Dixippus*, on the contrary, the extirpation of the corpora allata does not prevent the attainment of sexual maturity (Pflugfelder, 1937). Pflugfelder is inclined not to believe in the existence of too many hormones in insects. He thinks that the

hormone-concept ought not to be limited too narrowly in these animals, and that the action of the hormones is probably not as specific in lower animals as in vertebrates. In spite of this, the investigations reviewed here by Wigglesworth (1934, 1936), Weed (1936), and Pflugfelder (1937) show that the corpora allata produce hormones which act upon metamorphosis (as far as we know at present in Hemiptera and Phasmida, but not in Lepidoptera), upon sexual development (as far as we know in Hemiptera and Orthoptera Saltatoria, but not in Phasmida), probably upon metabolism, and possibly, though far from definitely proved, upon colour-change (cf. p. 88). It cannot be denied that if these functions are confirmed by future investigations, the corpora allata will in these respects show a certain physiological resemblance to the hypophysis in vertebrates.

Whereas several investigations have dealt with the function of the corpora allata as incretory organs, the corpora cardiaca, perhaps undeservedly, have been neglected. It is true that cyclic changes have thus far not been found in the corpora cardiaca, but Pflugfelder (1937) believes that in *Dixippus morosus* they have a secretory or excretory function. On account of their intimate relations to the aorta on one side and to the corpora allata on the other, they are perhaps also connected with the function of conveying to the nervous system stimuli resulting from changes in the composition of the body-fluid, whereupon an impulse to secretion under certain conditions would be sent to the corpora allata (Pflugfelder). As, further, the corpora cardiaca continue to grow very rapidly in the termite queens, Pflugfelder suggests that they might be connected with the increased metabolism of the fully mature queen. Finally, if, as a result of new investigations, the ring gland in the Diptera (cf. p. 54) is identified with the corpora cardiaca, as I have suggested, it seems possible that these organs, at least in the Diptera, are also connected with the hormonal regulation of metamorphosis.

There is no reason to regard the Verson glands as incretory organs, especially after the investigations of Schürfeld (1935) and Kühn-Piepho (1938). As to the function of the oenocytes and synoenocytes, only speculations can be found in the literature. Poisson (1924) believes these organs to be excretory and that they maintain the physico-chemical balance of the blood by means of absorbing some substances and secreting others into

it. This view was adopted by Boese (1936), who found that the oenocytes in larvae of Aphidae, Lepidoptera, and Coleoptera which had been infected with parasites change into curious giant secretory cells whose function it would be to maintain the normal balance in the blood. Rösch (1930) has found that in older workers of *Apis mellifica* both the oenocytes and the fat-cells join the wax-glands and empty their content into the latter —in this instance the function of the oenocytes must be clearly secretory and not incretory.

Other authors regard the oenocytes as incretory organs but have different opinions about their precise function. Weissenberg (1906) is inclined to connect them with metamorphosis, Stendell (1911, 1912) with increased blood-metabolism during metamorphosis, and Albro (1930) with moulting. Kreuscher (1922) believes the oenocytes to be incretory because their secretion is not fatty, and Wigglesworth (1933) regards the hormone of these organs as necessary for the synthesis of the non-chitinous substances of the cuticle. Zavrel (1935, 1938) detected in the oenocytes of Chironomidae cyclical changes which take place synchronously with the development of the genital ducts and the secondary sexual characters, and emphasizes the fact that the synoenocytes appear simultaneously with the maturing of the gonads and show a cyclical increase in size associated with each reproductive period in several insects. If this is true, it would confirm the hypothesis suggested by Harms (1914, 1926) and von Buddenbrock (1928) regarding the occurrence of incretory organs in insects locally separated from the sexual organs but exercising an influence on the development of the secondary sexual characters.

The corpus adiposum in insects has usually been regarded as a depot for fat and a seat of the synthesis of the substances which build up the body (Weber, 1933). In agreement with this hypothesis Teunissen (1937) has proved that the fat-body in *Calliphora* shows cyclical changes during the pupal stage, at which it absorbs substances from other degenerating organs, prepares them, and delivers the new substances to the growing organs. In addition to the extracts from the paper of Iwanoff & Mestscherskaja (1935) which have already been given on pp. 12 and 46 it must be mentioned here that these authors have found an incretory function of the corpus adiposum in the

Orthoptera, for in *Blatella germanica* this organ produces a secretion which increases the permeability of the eggs and thus promotes their maturation. The hormone is neither sex- nor species-specific, since extracts of the fat-body of the males also increase the permeability of larval ovaries, and the larval ovaries of *Blatella germanica* can be made to mature in the haemolymph of *Blatta orientalis* and *Locusta migratoria*.

Iwanoff & Mestscherskaja (1935) seem also to have found in the fat-body of *Blatella* a substance which stimulates the last moult, the metamorphosis moult. Extracts of the fat-body of mature female *Blatella* were injected into larvae which had passed the third larval moult. After the injection the male larvae completed their metamorphosis within 11, the female within 18 days, whereas the uninjected controls required 30–40 days to develop into imagines.

It may finally be added that Umeya (1926) suggests that the silk-glands in *Bombyx mori* may, besides their secretory function, possess an incretory importance in connexion with growth and metamorphosis. This view must be confirmed by further investigations.

VI

THE 'INTERNEPHRIDIAL' ORGAN IN GEPHYREANS (PHYSCOSOMA)

HARMS in 1919 and 1921 described an interesting organ in invertebrates which in several respects resembles the interrenal organ in vertebrates. In the worm *Physcosoma lanzarotae* which belongs to the Gephyrea there exists only one pair of 'nephridia' which, according to Harms, probably represent two fused pairs. Of these one pair has supplied the coelomic funnel and the ciliated canal, the other the end-tube, the terminal bladder, and the excretory canal. The end-tube is equipped with a tall renal epithelium which has an excretory function; it also contains some muscle-threads. The portion of the end-tube which is in direct continuity with the terminal bladder is surrounded by a peritoneal epithelium, and between this and the renal epithelium in the last two-thirds of the end-tube is

situated the 'internephridial' organ. The cells of this organ surround the renal cells in several layers, they are polygonal in form and filled with secretory granules which have different properties according to their age. The ripe secretion consists to a small extent of lipoid which is stained by Sudan III and is blackened by osmium; it is soluble in ether and chloroform and thus agrees with the lipoids in the inter-renal organ of vertebrates. Most of the secretion granules, however, are strongly refractive, not soluble in ether or chloroform, stain intensely with Heidenhain, safranin, and acid fuchsin, and consist of a nuclein-like substance. The ripe granules are secreted directly into the blood from the outer surface of the end-tube.

By appropriate experiments Harms has shown that it is probable that the internephridial organ performs essential functions. After extirpation of both internephridial organs the animal shows symptoms resembling those of Addison's disease and dies within a few days. If one internephridial organ and most of the other except a small portion is extirpated, the rest hypertrophies and the animal recovers. Finally, if both organs are completely extirpated but another organ is transplanted, the animal recovers if the transplantation is successful; a parabiotic fusion with a normal animal also keeps the operated one alive.

In another species of *Physcosoma*, *P. japonicum*, Koller (1935, 1936) has repeated the experiments of Harms but with different results. If the internephridial organ in *Physcosoma japonicum* is totally extirpated, this species can be kept alive for two weeks or more; it does not show the black colour (melanodermy) which, according to Harms, occurs in *Physcosoma lanzarotae* after this operation. Commenting on these investigations by Harms and Koller, von der Wense (1938) points out that in vertebrates also, different species behave in a very different manner after extirpation of the adrenal cortex, with which Harms has compared the internephridial organ of *Physcosoma*.

VII

THE CONTRACTING SUBSTANCE IN PHYSCOSOMA JAPONICUM. HEART HORMONES IN MOLLUSCA AND XIPHOSURA

IN the course of his experiments with *Physcosoma japonicum*, Koller (1936) detected that the 1–2 cm. long 'nephridial' tubes show rhythmic contractions with a frequency of 6–7 beats a minute. If several extirpated 'nephridia' are brought together in a vessel filled with sea-water the rhythm is considerably accelerated. A detailed investigation proved that in the nephridia, and also in the muscles and the nerve-ganglia, a substance is present which is able to increase the frequency of the contractions thirty times and to stimulate motionless nephridia to contract again. The active substance can be boiled without destruction and remains active in a dilution of 1 : 3,000,000, but could not be found in the blood.

In this connexion the investigations by Haberlandt (1930) of the 'heart-contracting hormones' in invertebrates may be mentioned. The contracting substance in *Physcosoma* and these 'heart hormones' belong according to Koller (1937) to the category of substances which he has called non-glandular tissue hormones.

Haberlandt had already found a substance in the heart of vertebrates which regulates the contractions and possesses several of the properties of a hormone, but is said not to be identical with the heart-activating substance of Loewi (cf. Loewi, 1935), which is the same as, or closely related to, adrenaline. Later, Haberlandt (1930) continued his investigations in invertebrates, especially in Mollusca (cf. also Willems, 1932). Haberlandt found that an isolated heart of *Helix pomatia* which had ceased to contract in Ringer solution again showed rhythmic contractions in alcohol- or water-extracts of the heart of other animals, whereas the same extracts of the foot-muscles were inactive. A heart hormone preparation of cattle, too, at a dilution of 1 : 1,000,000,000 still stimulated the pulsations in *Helix*. Dilute solutions of adrenaline likewise called forth weak contractions in *Helix*, but according to Haberlandt the heart

hormone in invertebrates is not identical with adrenaline, though this substance seems to exist in most (or all?) invertebrate groups. In agreement with the experiments upon *Helix*, isolated hearts of *Aplysia*, which had ceased to contract in body-fluid, began to show spontaneous and rhythmic contractions in extracts of a large heart of the same species.

Haberlandt (1931) also detected the heart hormone in the Xiphosura (*Limulus polyphemus*), which belong to the biggest living invertebrates. He proved that it was produced by the heart-muscles themselves and not in the heart nerve-ganglion; pure sea-water and extracts of the dorsal body-muscles were inactive.

It cannot yet be decided whether the 'heart hormone' which was investigated by Haberlandt is identical with a substance which circulates with the blood and also stimulates the heart-contractions. This latter substance was found by Blanc, Chambon, Jullien, & Morin (1932) in *Helix* and by Diederichs (1935) in *Mytilus*. Isolated hearts of *Helix* which were cut out during hibernation could be kept active for nine days in a sterile solution, containing Na, K, Ca, and Mg, during which time the average frequency was 15 beats a minute. When the contractions have ceased the heart can be brought to renewed activity in two minutes if some blood of *Helix* is added to the solution; after a few hours the frequency may rise to 12 beats a minute. Because the inactive heart was found to contain relatively large amounts of glycogen and the heart activity began after only two minutes, the renewed activity cannot be due to a supply of nourishment with the added blood.

Diederichs (1935) proved that an addition of sea-water (the inorganic composition of which agrees with that of the *Mytilus* blood) increases the tone of the *Mytilus* heart, whereas an administration of the blood of *Mytilus* increases the frequency of the heart-beats as well as the tone. As Koller (1937) points out, it seems improbable that this action is due to the presence of nutritive substances in the blood. Finally, Ungar & Zerling (1936) and Ungar (1937) have detected substances in the blood of Cephalopods after nerve stimulation which activate the heart (p. 139).

VIII

SOME HORMONES AND INCRETORY ORGANS IN CEPHALOPODA

ON account of their relatively considerable body-size, their highly developed nervous system and sense organs, their chromatophores, and lively motor activity, the Cephalopods have always been popular objects for anatomical and especially physiological investigations. This is also true for hormonal reactions and incretory organs. Some of these investigations, the paper by Sereni (1929) upon the development of the hectocotylus as a secondary sexual organ, and the detection by Ungar & Zerling (1936) and Ungar (1937) of a heart-activating substance in the blood, have already been mentioned briefly on pp. 31 and 76 (cf. also p. 139), and the accounts by Thore (1936) and Young (1936) of the corpus subpedunculatum and the corpus epistellatum are reviewed in connexion with the neurocrine organs on pp. 137 and 138. I intend to refer here to some other structures in the Cephalopods which probably or possibly function as incretory organs, and finally insert a short account of the phenomena of colour-change which in Cephalopods is in part hormonally regulated.

1. Corpus Branchiale

The corpus branchiale or branchial gland ('Kiemenbanddrüse') is situated beneath the branchiae (Hutchinson, 1928; Sereni, 1930), and consists of connective tissue and probably syncytial cells with vacuoles and eosinophil cytoplasm. It has an abundant supply of capillaries and is ductless. After extirpation of one of the bodies, the other gland is hypertrophied; if both are extirpated no other symptoms are observed except that growth ceases, whereas normal animals increase their weight five times in a comparatively short time.

2. The Pericardial Gland

The pericardial gland constitutes an appendix to the branchial heart and microscopically has the structure of a gland. It is possible, though far from certain, that the pericardial gland functions as an incretory organ (Kestner, 1931). The

pericardial gland is generally found in the Mollusca, but only in *Sepia officinalis* and its relatives is it concentrated into a distinct organ which can be extirpated. Kestner extirpated this organ on both sides. After a successful operation the animals behave normally for two days, but later become weaker and die within at most four days. If only one organ is extirpated the animals live a little longer, and injection of extracts of the pericardial gland seems to prolong life.

Finally, the suggestion of Sereni that the bursa fabricii in the Cephalopods also functions as an incretory organ may be mentioned.

3. Colour-change

Von Uexküll (1896) stated that a physiological colour-change under the influence of different illumination existed in the sea-urchin *Arbacia*, but Parker (1931) proved that this was not correct. Chromatophores are also found in a few Polychaeta, for instance in *Polydora*, but the most carefully investigated instances of physiological colour-change occur in the following groups of invertebrates: Hirudinea, Cephalopoda, Crustacea, and Insecta. In the Hirudinea (*Piscicola geometra*, *Glossosiphonia complanata*), which have very simple eyes but possess a reaction to light (Denzer, 1935), there is no adaptation to the colour of the background; the chromatophores are simply expanded in light and concentrated in darkness (Janzen, 1932, 1933; Wells, 1932). The factors which regulate the periodic expansion and contraction of the pigment granules in the *Hirudinea* have received no detailed investigation. In Crustacea and Cephalopoda as in the Hirudinea, the pigments of the skin which take part in the physiological colour-change are enclosed within special independent organs, the chromatophores, whereas in insects the pigment granules are distributed throughout the common hypodermis cells. Both in Crustaceans, in which the chromatophores are not innervated, and in insects, the physiological colour-change (and also at least to a considerable extent the morphological colour-change; see page 81) is regulated by hormones, whereas the chromatophores in the Cephalopoda have a special structure and, alone among invertebrates thus far investigated, are innervated.

The chromatophores of the Cephalopoda consist of sacs which

are filled with brown, red, or yellow pigment and are not able actively to change their form. The expansion and contraction is brought about by means of a system of radially extended muscle-threads which are attached to the periphery of the sacs parallel to the surface of the skin (Fig. 12). During the contraction of the muscles the chromatophores are extended in the same plane and the pigment is uniformly distributed; when the muscles slacken, the chromatophores are contracted to small spheres by their own elasticity (Bozler, 1928, 1931). Nerve-

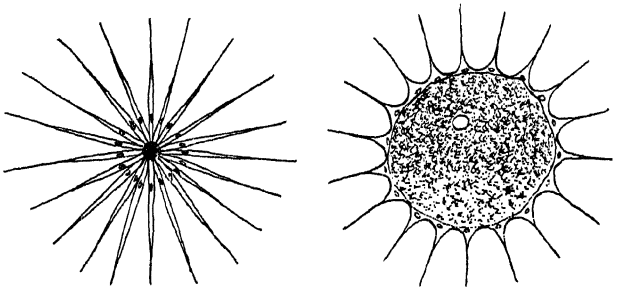


FIG. 12. Chromatophores in Cephalopods, schematically. *a* contracted, *b* expanded. In the latter instance the chromatophore muscles are maximally contracted. After Bozler.

fibres from the central nervous system innervate the chromatophore muscles without any intervening nerve-plexus (Hofmann, 1907, 1910). By various experiments Bozler proved that the nerve-fibres to the chromatophores must be of two different kinds, one which causes tetanic contractions, and another which decreases the tone of the chromatophore muscles. The expansion is due to a tetanic contraction which is caused by the action of the central nervous system. In the production of the colour in Cephalopods besides the pigments of the chromatophores, iridocytes and reflecting cells are also active (Schäfer, 1937, 1938), but they do not themselves take part in the physiological colour-change. Our detailed knowledge of the structure and innervation of the chromatophoral system in Cephalopods would seem to permit the opinion that the colour-change in these animals is completely regulated by the nervous system. In a long series of investigations in this field Sereni (1927–31) has, however, reached the following conclusions regarding the

connexion between the nervous and the chromatophoral systems in Cephalopods. The reactions of the chromatophores are influenced by three different nervous centres: (1) the motor centres (the B-centres) which are probably situated in the suboesophageal ganglia; (2) the common superior centre for the colour-change (the A-centre) which is probably situated in the central ganglia; and (3) a centre (the C-centre) which retards the expansion of the chromatophores and is probably situated in the cerebral ganglia. The movements of the chromatophores are thus regulated by antagonistic stimulating and retarding centres, but the activity of these centres and thus also the degree of the contraction and expansion of the chromatophores is influenced according to Sereni by antagonistic substances which circulate with the blood. These are tyramin and betain.

Of these two substances, tyramin (Henze, 1905, 1913) is a normal product of the posterior salivary gland (the poison gland), and is not only found in the saliva but also in the blood (cf. Ungar, 1937, p. 76), and is said to act as a stimulus on the B-centres or on the nerve-endings which reach the B-centres from the A-centre. According to Sereni (1928) tyramin, like adrenaline (p. 11), contracts the chromatophore muscles and thus expands the chromatophores. When Cephalopods eat they grow darker on account of the increased activity of the salivary glands, and thus if blood from an eating coloured *Eledone* is injected into a hungry light *Octopus*, the latter grows dark. That the tyramin is transported through the blood and is not species-specific was further shown by Sereni by parabiotic experiments. Betain has been found in the muscles of Cephalopods, but the source of its origin is still unknown (Henze, 1910). It acts antagonistically to tyramin, and Sereni suggests that both substances not only act indirectly by means of the central nervous system, but also directly on the denervated chromatophores. Ten Cate (1933) has supplemented the investigations of Sereni, finding among other things that adrenaline and acetylcholine act antagonistically on the muscles of the chromatophores, if applied to the stellar ganglion; in this instance the chromatophore muscles relax with adrenaline, the chromatophores are contracted, and the animal grows pale. After application of acetylcholine to the stellate ganglion the chromatophore muscles contract, the chromatophores are expanded, and the animal grows dark.

IX

HORMONAL REGULATION OF COLOUR-CHANGE IN INSECTS

SEVERAL insects are distinguished by beautiful colours which are either chemically produced pigment colours or physically produced structural colours (Weber, 1933). Of these only the first-named are of interest in this connexion. The pigment either occurs in the cuticle or the hypodermis, or is found in a subepidermal position. The pigments in the cuticle commonly play the most important part. They belong to the melanins which persist even after the death of the animal, which are produced again after each moult under the influence of oxydases and absorption of oxygen, and which can be deposited as granules both in the cuticle and in the cytoplasm of the hypodermis cells. These cells, however, often contain pigment granules of different origin which are less permanent and therefore rapidly fade after death. These granules may be yellow, green, orange, or red, and can be found as small droplets as well as granules.

As in Crustacea, there is in the insects a slower morphological and a more rapid physiological colour-change which, always in Crustacea and commonly in insects, is regulated by optic stimulation via the eyes and the nervous system. The morphological colour-change consists in a quantitative increase or decrease of the amount of the pigments, the physiological colour-change in a change in position of the different pigments under the influence of light, temperature, moisture, &c. A physiological colour-change which consists in an adaptation to the colour of the background has so far been detected among the insects in Culicidae, Lepidoptera, Orthoptera Saltatoria, and Phasmida. (Cf. Collembola; Handschin, 1926).

In the larvae of the Culicidae there is not only a typical morphological colour-change, but also, at least in *Corethra*, a rapid physiological colour-change which in this instance is limited to special pigment-cells of the air-sacs (Martini & Achundow, 1929). As in the Crustaceans, the persistent action of darkness in *Anopheles maculipennis* is not the same as removal to a dark background. In the former instance the animals

gradually become light brown, in the latter the larvae and pupae become very dark. *Culex pipiens* also shows a gradual adaptation of its colour to the background if young larvae are used for the experiment from the beginning. On the other hand, larvae of *Corethra* which are kept a longer time upon a white background grow thoroughly transparent, and if kept upon a black background grow 'smoky black'. In addition in *Corethra* there is a very rapid movement of the black pigment-cells on the air-sacs.

On a black background the black pigment-cells of the air-sacs are evenly distributed all over the surface of the air-sacs and are

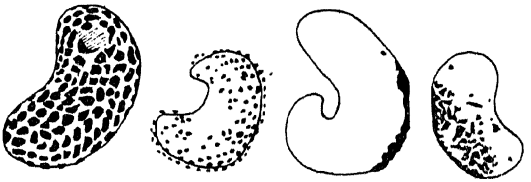


FIG. 13. Pigment cells of the air-sacs in *Corethra*. *a* upon a dark background; *b* after removal to a white background; *c* after complete adaptation to a white background; *d* a short time after removal from a white to a black background. After Martini-Achundow.

expanded, but after removal to a light background the pigment-cells contract and wander by amoeboid movements to a particular side of the sacs (Fig. 13). This constitutes in principle a new method of colour-change which is quite different from that already described in Cephalopods and that which occurs in Crustaceans; it also differs from the migration of the pigment granules within the hypodermis cells in the physiological colour-change of the skin in the Phasmida considered later on. It is evident that light stimulation through the eyes plays a part in the movements of the pigment-cells of the air-sacs in *Corethra*, and the experiments by Martini & Achundow (1929) make it probable that the brain is engaged in the reaction. This does not exclude a hormonal influence upon the pigment migration.

By various experiments Przibram (1922), Brecher (1924, 1925), and Giersberg (1929) have proved that certain Lepidoptera have a highly developed power to adapt the colour of the pupae to the colour of the surroundings, and that the eyes play

a decisive part in this process. If the eyes are extirpated or prevented from functioning through constriction of the head, larvae which are treated in this way assume upon any background the same colour as if kept in darkness. If, on the other hand, the eyes in *Pieris brassicae* are covered with a transparent yellow or blue dye, pupae of the same colour are produced as if the larvae had pupated in yellow or blue surroundings (Brecher, 1924, 1925). It is evident that a centre in the head is engaged in these processes, which centre is also influenced by temperature, because 'cool-forms' are produced if the head is kept cold (also if the body is simultaneously kept warm) and vice versa. Thus it is not the amount of warmth which reaches the body but the effect of the cold and warmth upon the head which decides the colour of the pupa (Giersberg, 1929).

In the migratory locusts (*Locusta migratoria*, *Locusta pardalina*) there is an individual adaptation to the colour of the background, and also it is found that there is a curious and considerable difference in colour between the solitary, non-migratory phase and the well-known migratory phase with its big swarms. According to the 'locustin theory' (Faure, 1932), the continuous activity of the migratory forms living in swarms leads to the production in the muscles and other organs of special substances ('locustin') that are deposited directly or indirectly in the skin as black pigment and cause the more intense and dark colour which distinguishes the migratory phase. In the red locust (*Nomadacris septemfasciata*) the same difference exists between the darker-coloured migratory phase and the solitary phase when the colour may be green, grey, brown, or yellow, but always lighter than in the former phase (Faure, 1935). The green colour seems to be the result of an abundance of succulent green food and a moist atmosphere; the grey, brown, and yellow are, according to Faure, probable produced by imitation of the colour of the background. Thus specimens of the red locust reared in cages painted white become much lighter than specimens reared in cages painted black. It is not known whether hormonal reactions play a part in these (morphological) colour-changes, but it seems very probable that this is the case.

In the Phasmida, which are fairly closely related to the Saltatoria, several authors have recently investigated the phenomenon of colour-change in *Dixippus morosus* (Giersberg,

1928, 1932; Atzler, 1931; Priebatsch, 1933; Hahna & Janda, 1934; Janda, 1935, 1936; Kalmus, 1938). *Dixippus* shows a morphological and a physiological colour-change which are both hormonally regulated. It possesses in the skin several different pigments, among which Schleip (1911–21) distinguished a brown, an orange, and a green pigment. Giersberg adds further a yellow one, in addition to which according to Schmied (1937) comes a bright-red pigment spot on the inner side of the base of the first leg in the mature females (cf. p. 59).

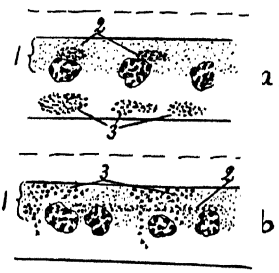


FIG. 14. Position of pigments in the skin of *Dixippus morosus* in light (*a*) and in darkness (*b*). *1* green and yellow, *2* orange, *3* brown. After Giersberg.

According to Schleip and Giersberg the brown pigment is melanin and the orange and the yellow are lipochromes, whereas the green, which was regarded by Schleip as a lipochrome, must, according to Giersberg, be something else; its real nature is still not discovered. The very limited pigment spot at the base of the female first leg may be a carotinoid (Schmied, 1937). All pigments are found as granules within the cytoplasm of the common hypodermis cells, and independent chromatophores as in Cephalopods and Crustaceans do not exist.

Among the common pigments which occur in both males and females the brown melanin and the red lipochrome migrate during the physiological colour-change in a characteristic manner, whereas the green and yellow have a permanent position (Fig. 14). The migration of the brown and red pigment is dependent upon the light; the animals are thus dark by night and pale by day, which periodicity is repeated in constant darkness but after some time can be reversed, if the animals are kept in light by night and in darkness by day (Kalmus, 1938). At a constant moisture and in light, white and light-yellow backgrounds act as white surfaces, black and red as dark surfaces. Upon the former, *Dixippus* grows pale, on the latter dark. In physiological colour-change moisture induces darkening within 30–60 minutes, dryness discolouring within 1–2 hours. Under the influence of ether, pressure, wounds, and injection of dis-

tilled water, the animals grow dark, whereas injection of 2 per cent. NaCl-solution makes them pale. In morphological colour-change, optic stimulation, nutrition, and temperature are active, and according to Giersberg (1932) physiological and morphological colour-change are two sides of the same phenomenon, which is connected with changes in the metabolism and is probably due to a variation of the amount of hormones in the blood, involving production and destruction of the active substance which is the cause of the colour-change.

That physiological colour-change in *Dixippus* is actually regulated by a hormone was made probable by various experiments

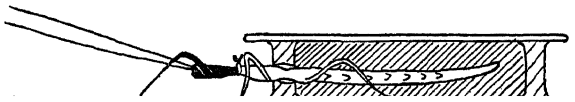


FIG. 15. *Dixippus morosus* with the posterior portion of the body in a moist chamber. Behind the head a ligature. After Giersberg.

by Giersberg (1928). Giersberg constructed a moist chamber in which the animals could be inserted more or less completely at will. If the abdomen of a normal animal is put into the chamber whereas the head and thorax remain in the open air, the animal darkens within 30–60 minutes. In spite of the fact that the moisture acts on the hind end of the body by means of the tracheal nerves, the darkening begins at the head and extends backwards. If, on the other hand, the animal is constricted around the thorax and then inserted into the moist chamber the hind end of the body, which is in moisture, remains pale as in the first instance, whereas the anterior end in front of the constriction, which is in comparatively dry air, grows dark (Fig. 15). If the ligature is loosened the darker colour extends backwards without hindrance. In other experiments instead of making the constriction, Giersberg cut the nervous connexions between the brain and the suboesophageal ganglion, or between this and the ventral ganglia. If after the shock had disappeared, such an animal was put into the chamber head first, it behaved normally and darkened from the head backwards until the whole body was dark. But if the same animal was inserted with only the posterior end (behind the place of the operation) in the chamber, it remained pale.

These experiments by Giersberg show that the constriction in the first instance prevented free circulation between the anterior and posterior portions of the animal, but did not affect nervous transmission. The stimulus from the moisture acts on nerve-endings in the abdomen, and is transferred to a centre for colour-change in the brain. This acts upon an incretory gland whose secretion affects the migratory pigments if the circulation is free. When, on the other hand, the nervous connexion is interrupted, the stimuli of moisture which acted upon the abdomen cannot reach the colour-change centre, and no pigment migration can take place if only the hind end of the body is inserted into the moist chamber; if the anterior end instead is put into the chamber, the pigment migration takes place as in normal animals.

By means of other experiments, Janda (1935, 1936) confirmed the hypothesis of a hormonal regulation of colour-change in *Dixippus*. Thus he found that transplanted portions of the skin showed a normal colour-change synchronous with the host after 2–3 days, during which time a nervous connexion between the transplant and the nervous system would hardly have been established (though it must be very difficult to prove histologically the presence or absence of such a connexion). Janda further replanted the head + prothorax in *Dixippus*, and was able to keep such animals alive for 40 days and more. In specimens with weak or dying head-transplants, the body assumed a very light colour (as after complete extirpation or constriction of the head), and the pigment migrations disappeared. If the replantation succeeded the colour-change returned after a certain time before a nervous connexion could have been established; later, this physiological colour-change could, in a few instances, be observed daily during three weeks.

In the physiological colour-change in *Dixippus* the temperature, osmotic, and tactile stimuli are direct and independent of the central nervous system; they mostly only act locally, whereas optic and moisture stimuli act indirectly by means of the central nervous system. Giersberg (1928) was the first to try to localize the centre of the colour-change by means of various experiments, which were later continued by Atzler (1930). According to Atzler the nervous centre for colour-change is situated in the 'Dritthirn' and the incretory gland connected with the same

phenomenon in the tissue on the dorsal side of the ganglion frontale in front of the brain. Przibram & Suster (1931) have objected to this hypothesis that as a result of Atzler's operation, the animals only lose the power of conducting optic stimuli and thus the conclusions regarding the position of the nervous centre and the incretory organ are not decisive. Though the experiments of Atzler seem to show that neither the extirpation of the corpora cardiaca, nor that of the corpora allata have any influence upon colour-change, my own just published (1938) investigations prove that, on account of their structure, probably no other organs of the head except the corpora cardiaca and the corpora allata can be regarded as having an incretory function (Plate III). Atzler also calls the antennal ganglia, the deutocerebrum, by the name of 'Dritthirn', which term ought to be reserved for the tritocerebrum; but more important is the fact that on the dorsal side of the ganglion frontale no structures other than muscles, tracheal ramifications, and tissue, belonging to the aorta, can be found. Thus in histological preparations it is not possible to detect any incretory structures in the position indicated by Atzler. This does not mean that the scheme put forward by Atzler for the conduction of tactile and optic stimuli in respect of pigment migration may not be correct. It runs thus: Nervous system–incretory gland–blood transportation. The same scheme for the influence of moisture upon the colour-change would be: tracheal air–nervous system–incretory gland–blood transportation.

Since the investigations of colour-change in *Dixippus* prove that somewhere in the head of this species there must be an incretory organ which secretes a pigment-activating hormone, it is of interest that I (1936–38) detected in the head of several species of insects a substance which after injection into shrimps (*Palaemonetes vulgaris*, *Leander adspersus*) is able to concentrate their red and yellow pigments. This faculty was especially strongly developed in the Orthoptera Saltatoria, but was also very evident in the Phasmida (*Diapheromera femorata*, *Dixippus morosus*), and in the latter group has been confirmed by Kalmus (1938) in *Dixippus*, after injection into *Astacus vulgaris*. According to Kalmus it is possible that by night the amount of the active substance which is found in the blood is larger than by

In some experiments of mine—just published, I have

found that this substance in *Dixippus* is produced in the posterior half of the head, whereas extracts of the anterior half are inactive in respect of the contraction of the red and yellow pigments in *Leander adspersus*. Thus it seems probable that either the corpora cardiaca or the corpora allata are the source of this substance, since these organs are the only incretory structures in the insect head thus far identified, and in *Dixippus* are situated in the posterior half of the head (Plate III).

It is still not certain whether the substance in the head of *Dixippus* which contracts the red and yellow chromatophores in shrimps has anything to do with the colour-change in *Dixippus* itself. Kalmus (1938) was unable to exert any influence upon the pigment migration in *Dixippus* with extracts of its own head, and my own investigations have thus far been inconclusive on this point. But since the mechanism of pigment migration in Insecta and Crustacea is quite different, the latter animals possessing anatomically independent and rapidly reacting chromatophores, it is possible that it is necessary to repeat the injections regularly in the same animal for several days to obtain positive results in *Dixippus*. Thus it might be premature to deny the identity between the substance in the head of *Dixippus* which is able to contract the chromatophores in shrimps and that which regulates its own pigment migration. It seems at least certain that the substance in the *Dixippus* head which contracts the chromatophores in shrimps has several properties in common with the pigment-activating hormone of the Crustaceans. Thus it can be considerably diluted and boiled without losing its pigment-activating power, and just as the colour-change hormone of Crustaceans contracts the chief chromatophores in shrimps but expands the chief chromatophores in crabs (cf. p. 105), extracts of the head in insects according to unpublished experiments by Carlson have exactly the same effect on the crustacean chromatophores.

X

THE SINUS GLAND AND COLOUR-CHANGE IN CRUSTACEA

ALTHOUGH it is possible to produce extracts of different organs in the Crustacea (ganglia, rostral portion of the cephalothorax) which possess an influence on the contraction and expansion of the chromatophores, the chief source of the pigment-activating substance (the chromatophorotropic hormone) is the eye-stalk of higher stalk-eyed Crustacea (Perkins, 1928). According to Hanström (1935, 1937) the incretory organ in the eye-stalk which is responsible for secreting this substance into the blood (p. 119) is the blood gland or sinus gland; on account of its connexions with the central nervous system and the circulating system it shows certain resemblances to the choroid plexus of the vertebrate brain.

1. The Sinus Gland

The sinus gland of Crustacea was detected by Hanström (1933) and has later been described in detail by Sjögren (1934), Hanström (1937), and Ståhl (1938). Further statements will be found in a paper by Carlson which will soon be published.

According to Hanström (1937), the sinus gland occurs in its most primitive form in the Mysidacea (*Boreomysis arctica*, *Eucopia*). It is situated on the lateroventral side of the eye-stalk (when this is extended laterally) and consists simply of a thickened disk-shaped portion of the nerve-sheath (the neurilemma) of that part of the brain which is situated within the eye-stalk (Plate IV. 1). In *Eucopia* this thickened portion lies on the inner side of the thin limiting membrane of the neurilemma, and thus on this side is surrounded by nerve-cells; on the outer side it adjoins the big blood-sinus of the eye-stalk. The wall of the sinus gland is traversed by radially arranged secretory canals which are filled with eosinophil droplets and open out into the sinus. The large nuclei are situated on the inner side of the secretory tissue, and the gland receives a nerve from the medulla terminalis, a centre of the brain which together with the primary optic centres (lamina ganglionaris, medulla externa, and

medulla interna) has wandered out into the eye-stalks in higher stalk-eyed Crustacea and is connected with the rest of the protocerebrum by means of the pedunculus lobi optici.

A sinus gland of essentially similar structure as in *Eucopia* has been detected in the Euphausiacea (*Meganyctiphanes norvegica*) by Carlson and will be described in his forthcoming paper. In the sessile-eyed Isopoda (*Oniscus murarius*) and Amphipoda (*Gammarus locusta*), Ståhl (1938) has found small organs of the same kind situated in the nearest vicinity to the optic centres but more distinctly separated from the lobus opticus. They are, however, both connected with the neurilemma and adjoin a blood-sinus of the head.

In the Decapoda, too, the sinus gland must originally have been intimately connected with the neurilemma though it has later detached itself and is only connected with the wall of the sinus. In several shrimps, for instance *Palaemonetes vulgaris*, the sinus gland retains its primitive situation on the neurilemma, its structure only being complicated by a blood-vessel which passes through the gland on its way to the blood-sinus (Plate IV. 2). The sinus gland in the Decapoda is commonly found within the eye-stalks as in Mysidacea, Euphausiacea, and Stomatopoda, but in several Anomura with more or less reduced eyes the sinus gland is situated in the head close to the brain.

The muscles, nerve-centres, and other organs of the stalked decapod eye commonly receive the blood through an arteria optica and an arteria oculomotoria (Bouvier, 1891; Bernhards, 1916; Balss, 1927). According to Brody & Perkins (1930) in *Palaemonetes vulgaris* there exists only an arteria ophthalmica which constitutes a branch of an unpaired artery of the rostral region. According to Sjögren (1934) two radially arranged sinuses between the medulla externa and the medulla interna and which are situated within the neurilemma, one dorso-laterally, the other ventro-medially belong to the venous system. These transport the blood from the nerve-centres of the lobus opticus into the large outer sinus situated between the lobus opticus on one side and the wall of the eye-stalk on the other. The common position of the sinus gland in the Decapods is at the point where the dorso-lateral inner sinus opens out into the outer sinus. It is situated here in *Palaemonetes vulgaris*, constituting a cup-shaped structure around the opening of the inner into

the outer sinus (Plate IV. 2). It thus represents a further development and a differentiation of the wall of the neurilemma, which in common histological preparations looks like a structureless membrane with rather widely separated flat nuclei. In the place where the combined neurilemma- and sinus-wall is changed into the sinus gland it assumes a syncytial structure and thickens, whereas the nuclei become round like balls and increase in number. The structureless membrane remains on the peripheral side, whilst the inner side where the nuclei are situated close to the nuclei of the nerve-cells is not sharply limited. The wall of the gland contains radially arranged secretory canals and small droplets of different size which stain an intense red with eosin and acid fuchsin, and bright green with 'Lichtgrün'. The nerve, which especially in the crabs (Plate VI), and in the Reptantia Astacura (Plate V. 1) is often composed of very coarse fibres, originates in the medulla terminalis.

In some shrimps (*Acanthephyra purpurea*) a higher morphological development of the sinus gland is reached through the freeing of the gland from direct communication with the neurilemma and a simultaneous involution of its wall (Plate IV. 3). In this manner a more or less rounded sac is formed which has the structureless membrane on its inner side and receives the nerve from the outer. The gland is still connected with the small inner sinus on one hand, with the big outer sinus on the other. A further complication of structure is found, especially in larger Decapods, when the inner dorso-lateral sinus branches near its opening, while the glandular wall extends over the proximal portions of the branched sinus and thus itself assumes a ramified form. In this instance also, as in most crabs, the wall encloses a space which is limited by the structureless membrane. If the branching of the inner dorso-lateral sinus is very well developed, as in *Cambarus*, *Astacus vulgaris*, and *Homarus americanus* (Plate V. 1), the cavity of the gland is thoroughly split up and the organ assumes a complicated corrugated form, some portions of it projecting into the outer sinus, others surrounding the proximal parts of the branches of the inner sinus.

Finally, in several Anomura with reduced eyes the sinus gland is no longer found in the eye-stalks but within the head. In these, for instance, species of *Hippa*, *Emerita*, *Gebia*, *Gebiopsis*, *Calocaris*, and *Callianassa*, the structure of the gland has probably

been secondarily simplified. The gland-wall is connected with the neurilemma of the brain and adjoins a large blood sinus, but it has no connexion with an inner sinus (Plate V. 2). This has probably been reduced in connexion with the reduction in size and differentiation of the optic centres. Nevertheless, the sinus gland in these Anomurans is not flat as in the Mysidacea, but is sharply separated from the brain. It has the structureless membrane on the outer side, and has no free space in the inner. Thus the secretory tissue is situated on the inner side of the membrane and, further in, there is connective tissue together with the endings of the sinus-gland nerve. On account of this special structure I have called this type of sinus gland 'everse', since the structureless membrane is located in the periphery, whereas the type earlier described in most shrimps, prawns, and crabs is called 'inverse', since the same membrane here surrounds a free central space.

If a sinus gland of the simple disk-shaped form which is found in the Mysidacea (Plate IV. 1) is accepted as a starting-point for all the different types of this organ which exist in the Decapoda, the inverse type (Plates IV. 2, 3; VI), is developed when the peripheral portions of the disk are bent upwards, at first cup- (Plate IV. 2) and then more or less ball-shaped; thus enclosing a smaller portion of the original cavity of the big outer blood-sinus (Plates IV. 3, VI). In this instance the structureless membrane is applied to the interior and the endings of the sinus nerve surround the secretory tissue from outside. The everse type of sinus gland is developed when the central portions of a disk-shaped gland rise above the peripheral portions, the membrane surrounds the secretory tissue from outside, and the nerve-endings enter it from the inner side (Plate V. 2). The unusually rich branching of the proximal portions of the inner dorso-lateral sinus which results in the corrugated form in such Decapods as *Cambarus* and *Homarus* makes this kind of sinus gland neither typically inverse nor typically everse (Plate V, 1).

In the highly developed inverse sinus gland of *Callinectes sapidus* its finer structure can be more easily observed than in other Decapods (Plate VI). The wall of the gland in *Callinectes* is very thick, and the nuclei are situated at the same level in the middle of the secretory tissue. Between the portions of the wall which belong to the different nuclei no cell boundaries can be

observed with ordinary staining methods. Situated close to one another are the secretory canals which in *Callinectes* have a wider rounded peripheral end and contract towards the structureless membrane, thus assuming a bottle-shaped form. The canals open into the free space of the gland, and the openings can be observed on the surface of the structureless membrane as fine, intensely stained points. From the cavity of the sinus gland the secretion can be transported without difficulty into the outer blood-sinus of the eye-stalk.

There also exists a sinus gland resembling the inverse type of the Decapoda in all Stomatopoda thus far investigated (Hanström, 1937). From the lateral side of the medulla terminalis a thick nerve runs to the wall of a large blood-sinus beneath the eye, and the portion of this sinus which is situated between the medulla externa and the medulla interna is developed into a sinus gland. In most species, for instance *Squilla mantis*, the sinus gland has no direct connexion with the neurilemma but is extended over a certain portion of the sinus wall itself and the proximal portions of some vessels which correspond to the inner dorso-lateral sinus in the Decapods. The finer structure of the gland is the same as in the latter Crustacea.

2. Colour-change

A. The Hormonal Method of Colour-change in Crustacea. Among several higher Crustacea (Isopoda, Amphipoda, Mysidacea, and Decapoda, especially shrimps) there is a surprisingly rapid and strong colour-change whose efficiency is inferior only to that of Cephalopods and chameleons. It consists mostly in an adaptation of the colour of the body to the colour of the background through the concentration of some pigments and dispersal of others. This occurs in *Palaemonetes vulgaris* (Perkins, 1928; Brown, 1933–5) and *Crangon vulgaris* (Koller, 1925–30), whereas in other Crustacea such as *Uca* (Megusar, 1912; Carlson, 1936; Abramowitz, 1937), and *Leander squilla* (Hanström, 1937), the colour-change manifests itself in periodical contractions and expansions of the chromatophores, independently of the light and the colour of the background. In these instances the red and yellow pigments are dispersed by day and concentrated by night, thus showing a daily rhythm.

The first published instance of colour-change in the Crustacea (cf. Rynberk, 1906) is said to be that of *Hippolyte* (Kröyer, 1842), and the first description of chromatophores in these animals that of *Mysis* (Sars, 1867). The chromatophores in Crustaceans contain several nuclei, and according to Degner (1912) must be regarded as syncytial structures. According to Matzdorff (1883) the branches of the chromatophores are amoeboid, being temporary portions of the chromatophores

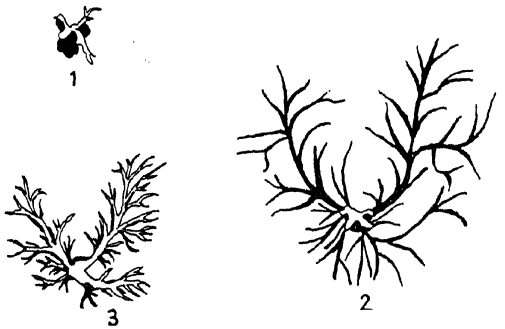


FIG. 16. The same chromatophore in *Crangon vulgaris* in an animal kept upon white (*1*), dark grey (*2*), and yellow (*3*) background. Melanin black, yellow pigment white. Simplified after Koller.

developed during their expansion. The investigations of Keeble & Gamble (1900), Fröhlich (1910), Franz (1910), Perkins (1928), and, not least, Degner (1912) proved, however, that the migrations of the pigment granules depend upon intracellular protoplasmic streamings within preformed processes of the chromatophores, the chromorhizae. In the dispersal of the pigment the granules thus flow in a centrifugal direction; in concentration, in a centripetal. The chromatophores are often polychromatic and contain more than one pigment, for instance black, red, and yellow at the same time. The different pigments are, however, not mixed—the granules flow along different chromorhizae, separate from or parallel with one another (Fig. 16). Thus dispersal of a certain pigment in a chromatophore does not necessarily involve dispersal of other pigments contained in the same chromatophore, and if the pigments are all concentrated, the black, red, and yellow granules lie accumu-

lated in separate lumps in the centre of the chromatophore net (Fig. 16).

After covering the eyes with an opaque paint, or extirpation, Crustaceans lose the power of adapting their colour to the background, as was shown for the first time by Pouchet (1872). Thus in some way or another, optic stimuli must exercise an influence upon the expansion and contraction of the Crustacean chromatophores, and at first it was believed that these structures were innervated, just like the corresponding organs in Cephalopods. Although Pouchet (1876) himself believed in the innervation of the chromatophores, he was not able to interfere with the colour-change by nerve transections. The same results were obtained by Mayer (1879), Matzdorf (1883), Fröhlich (1910), Menke (1911), Degner (1912), Koller (1925, 1927), and Perkins (1928). Degner also tried to solve the problem by histological methods, because Retzius (1890) was the first biologist (and so far the only one) to believe that by means of the methylene blue method he had seen nerve-endings upon the chromatophores. Mayer believed like Pouchet in the innervation of the chromatophores and writes, 'The existence of an innervation is shown, without doubt, by experiments upon blinded animals'. But when he repeated the experiments of Retzius, using the same histological method, he was not able to confirm Retzius's results.

Koller (1925, 1927) repeated on *Crangon* the experiments made by Menke (1911) on *Idothea*, cutting the nerve-cord at different places. After this operation, too, those portions of the body which were situated behind the cut showed an undisturbed colour-change. Nor had transections of the peripheral nervous system any effect upon the same phenomenon. Koller concluded that substances in the blood must be responsible for the regulation of the colour-change and he was the first to try by blood transfusions to prove that the expansion and contraction of the chromatophores in Crustacea is hormonally regulated. 'According to the experiments described', he writes in 1929, 'there must, in all probability, be incretory organs which secrete special substances (hormones) into the blood after stimulation from the eyes, and this stimulation is transported by means of the central nervous system. The hormones are then transferred with the blood to the chromatophores and act upon the pigment migration.'

The term 'internal secretion' was already used in 1910 (though with another meaning) in connexion with chromatophoral functions in Crustacea by Doflein, who alluded to the production of the blue pigment in shrimps. This blue pigment is in most species developed in connexion with the contraction of the red and yellow chromatophores which, after the animal has been put into a light dish, become surrounded by a bluish cloud which permeates the surrounding tissue. The cloud increases for some time but gradually vanishes simultaneously with the concentration of the red and yellow pigments. According to Keeble & Gamble (1900–10) the blue coloration (which does not consist of granules) is derived from the red pigment, an opinion confirmed by Brown (1935) in *Palaemonetes*; Koller (1936), however, regards the yellow pigment as the source of the blue coloration in *Leander adspersus*. It must, however, be observed that the chemical composition of what are called brown, red, and yellow pigments in the shrimps is in most instances unknown. Doflein (1910) writes about this blue pigment: 'The investigations of Keeble & Gamble have led these authors to believe that the pigments in higher Crustacea are necessary substances in the metabolism, comparable with secretions, and that the chromatophores in certain respects may be compared with glands. I fully agree with them and would say that the production of the blue pigment and its permeating the tissues constitute an instance of internal secretion which can be directly observed' (cf. p. 103). A more or less permanent blue pigment is also often found in lower Crustacea, for instance in *Diaptomus superbus* (Copepoda), and can here be transformed into a red (cf. Brehm 1938).

In the blood transfusions made by Koller, blood from an animal (*Crangon*), which had been black-adapted through expansion of the dark chromatophores on a dark background, was injected into a light animal, which had been white-adapted through contraction of the same chromatophores on a white background. After the injection the light animal was again transferred onto the white background but assumed within 10–20 minutes a black colour in spite of the background-action. As a control, blood from a light-adapted animal was injected into another light-adapted shrimp without any reaction of the chromatophores. According to Koller the reversed experiment

did not succeed in *Crangon*; blood of a white-adapted shrimp injected into a dark-adapted one which was later transferred to the black background gave no reaction. Carlson, however, who has repeated these experiments in an investigation not yet published did not observe any darkening in a white-adapted *Crangon vulgaris* which was injected with blood from a black-adapted animal, but noticed that a black animal grew paler after injection of blood from a white. This is more in agreement with our knowledge of the colour-change mechanism in other shrimps.

Using rather different methods, Perkins (1928) proved that the colour-change in *Palaemonetes vulgaris* depends upon a substance which circulates with the blood. When the ventral ganglionic chain was severed in the region between the thorax and abdomen no observable effect could be found in subsequent chromatophore reactions. Other nerve transections, except such as passed through the dorsal blood-vessel, were also without effect. Whenever this vessel or its branches were severed, the chromatophores of those regions supplied by the severed vessels, if they were not already expanded, quickly passed into that state. As histological preparations did not show any trace of nerve-fibres accompanying the vessels and supplying the chromatophores, Perkins concluded that the agent controlling the chromatophore action must be some constituent of the blood itself. Finally, he was able to show after making different extracts of the body organs that the eye-stalk in *Palaemonetes* contains a substance which, injected into dark-adapted shrimps, contracts the red and yellow chromatophores even on a black background (cf. Plate VIII). The presence of such a chromatophore-activating substance, concentrating the red and yellow pigments in shrimps (but expanding the black and red pigments in crabs; cf. p. 104), has since been confirmed in several other species of higher Crustacea by Koller (1929), Koller & Meyer (1930), Smith (1930), Perkins & Kropp (1932), Hosoi (1934), Stephensen (1934), Hanström (1935, 1937), Carlson (1935, 1936), and Abramowitz (1936); compare also Koller (1936), Kleinholz (1937), and Ståhl (1938), who mostly deal with colour-change hormones in lower Crustacea Malacostraca.

B. Direct and Indirect Stimulation of Crustacean Chromatophores. Whereas some authors believe that the Crustacean chromatophores can be directly stimulated by light and

temperature (Gamble & Keeble, 1900; Megusar, 1912; Bauer & Degner, 1913; Smith, 1930, Giersberg, 1931), others (Matzdorff, 1883; Taite, 1910; Koller, 1927; Perkins, 1928; Parker, 1930) maintain that this is not the case. Smith (1930) detected that the chromatophores in *Macrobrachium acanthurus* expand in water of a temperature between 6 and 15 and between 35 and 40 degrees Celsius independently of the background colour. Between 15 and 35 degrees the chromatophores expand upon a dark and contract upon a light background. Smith then made extracts of eye-stalks of animals which had grown dark in cold water and of those which had grown dark in warm water, and injected these into dark-adapted animals which were kept at a normal temperature. In both instances the chromatophores contracted, and thus Smith concluded that the reaction of the chromatophores in *Macrobrachium* against warmth and cold was direct, since the animals still possessed a sufficient amount of pigment-activating hormone in the eye-stalks. This interpretation is not conclusive, since the hormone might very well be kept in store in the incretory gland of the eye-stalk without being released into the circulation if its nerve-centre exercised a retarding action upon the gland. Thus abnormally high or abnormally low temperatures could act indirectly by means of the nervous system, and primarily they would affect the nervous centre of the colour-change gland in such a manner as to prevent the release of the hormone.

In specimens of *Palaemonetes vulgaris* with unimpaired vision, the white (or rather light yellow) chromatophores, contrary to the red and yellow, are commonly contracted on a dark background and expanded upon a white in light, whereas they are contracted in darkness. After extirpation of the eyes the red and yellow chromatophores are maximally expanded independently of light and background, whereas the white in at least half the number of the experimental animals retain their full power of expansion and contraction. The white chromatophores in such animals behave as in normal individuals except for the fact that they lack the background adaptation. Thus on a dark background they do not contract as in seeing animals; the sole active factor which regulates their movements is light. Independently of the colour of the background, the white chromatophores in eyeless animals expand at high and contract at low light in-

tensity as if they were a kind of 'independent effectors' (Parker, 1919) reacting directly to light. Brown (1935) has, however, detected substances which contract the white chromatophores both in the eye-stalks and in the rostral portion of the cephalothorax. In the latter there persists also in adult individuals of *Palaemonetes* a nauplius eye (median eye) which is probably still functional. It is therefore possible that in this instance also, optic stimulation can be conducted via the nauplius eye and the brain to the organ in the cephalothorax which secretes the substance that acts upon the white chromatophores. Thus it is possible, though not yet definitely proved, that the contraction of the white chromatophores is also hormonally regulated in blinded animals (Hanström, 1937).

C. **Colour-change in Different Groups of Decapoda, Natantia, Reptantia Astacura, Reptantia Anomura, and Reptantia Brachyura. The Multiple Theory and the Unitary Theory of Pigment Hormones.** In respect to colour-change, the Decapoda Natantia (shrimps and prawns) that have been investigated in most detail are *Crangon vulgaris* from Europe and *Palaemonetes vulgaris* from North America. In *Crangon* (Koller, 1925–30) there are four different pigments in the chromatophores: sepia brown, white, yellow, and red, occurring in increasing amounts in this order. All four pigments can occur in the same chromatophore, whereas monochromatic chromatophores are always sepia brown (= melanin according to Verne, 1921). After experiments with differently coloured backgrounds and backgrounds of different light intensity, Koller proved that *Crangon* is able to accommodate its colour to white, black, yellow, orange, and red backgrounds through dispersal of some and concentration of other pigments; in which process the wavelength of the reflected light from the background, and not the light intensity, is the sole and decisive factor (Fig. 16).

The fact that *Crangon* is able to adapt itself to backgrounds of different colours according to Parker (1930) supports the theory that more than one hormone is concerned in the regulation of the pigment movements in shrimps. A hormone chiefly concerned with pigment concentration was found by Koller (1929, 1930) in the eye-stalks of *Crangon*, after Perkins (1928) had detected the same hormone in the eye-stalks of *Palaemonetes*. When Koller injected extracts of the eye-stalks of

Crangon into black-adapted individuals of the same species, he noticed a strong concentration of melanin and of the yellow pigment, but at the same time a dispersal of the white. For the white pigment this result is opposite to that found after extirpation of a certain region of the eye-stalk in the neighbourhood of the basement membrane of the eye, where, according to Koller, the pigment-concentrating 'white-organ' is situated. In this instance both the melanin and the white pigment were dispersed.

Koller has also made several experiments with the 'black organ' in *Crangon*, extracts of which are said to expand the black and red pigments in this species, and which is situated in the rostral region in a medial and dorsal position. According to Koller an administration of this organ *per os* also causes an expansion of the black pigment, whereas feeding with other portions of the body gave no results in this respect. Extirpation of the rostral black organ prevents the expansion of the melanin, but pressure upon this region causes its expansion. Beauvallet & Veil (1934) have confirmed the fact that extracts of the rostral region cause expansion of the pigments in *Palaemon* (*Leander*) *squilla*, but they add that an extremely high concentration is needed. Perkins & Snook (1931) and Kropp & Perkins (1933), on the contrary, were not able to verify the existence of a rostral black organ in the American species closely related to the European *Crangon vulgaris*, and Carlson did not get any conclusive evidence during his investigation of the latter in his as yet unpublished study of the colour-change in several species of Swedish Decapods. During my investigation of American Decapods (1937) extracts of the rostral region of *Cambarus*, injected into *Palaemonetes vulgaris*, did not cause any expansion of the pigments, and extracts of the anterior part of the cephalothorax of *Gebia affinis* and *Hippa talpoida* contracted the red and yellow chromatophores, because the pigment-concentrating hormone which in most Decapods comes from the eye-stalks has its source in the head in these species (cf. p. 121).

According to the comprehensive paper by Koller (1937) the source of the melanin-expanding hormone in *Crangon* might possibly be found in the lymph glands described by Cuenot (1891), Bruntz (1907), and Kollmann (1908), or in the median eye (the nauplius eye) or the medial frontal organ, which structures often persist in this region of the cephalothorax in adult

Decapods. In the same work Koller gives the precise number of substances which seem to act upon the chromatophores in *Crangon* as three. The hormone of the rostral black organ would expand the melanin, the pigment-concentrating hormone in the eye-stalks would concentrate it, and a special substance of doubtful origin would expand the yellow pigment. For the localization of the pigment-concentrating hormone cf. p. 119.

In the chromatophores of *Palaemonetes vulgaris* there are three different pigments, red, yellow, and white (as seen in reflected light; in certain circumstances it looks light yellow). The black pigment melanin, which is common in the Brachyura, seems rarely to occur in the Natantia; in fact it has probably not been identified in shrimps other than *Crangon* (Verne, 1921). The red and yellow pigments mostly occur in the same chromatophores in *Palaemonetes*, but constitute independent pigment lumps when concentrated; the white pigment is always found alone (Perkins, 1928; Brown, 1933–5).

Chemically the red pigment of *Palaemonetes* should be identical with astacin and the yellow with plant carotin. The white pigment has not been investigated chemically in *Palaemonetes*, but according to Mollitor (1937) it is composed of uric acid in *Eriocheir sinensis*. The antennal glands are supposed to be the chief excretory organs in Decapods, but their secretion contains very small amounts of nitrogen, though *Eriocheir* is chiefly a flesh-eater. Thus Mollitor examined the different organs in respect to their percentage of nitrogen and found considerable amounts of aminoacids (the mother substance of the melanins) and uric acid in the hypodermis cells, the uric acid chiefly occurring as solid granules in the white chromatophores. The hypodermis is consequently to be regarded as the chief excretory organ for ammonia and uric acid, the uric acid being stored as the white pigment, which in *Eriocheir* (contrary to the condition in insects) is not lost at the moults.

The red and yellow chromatophores in *Palaemonetes* are about evenly distributed all over the body (cf. Plate IX. 1), whereas the white are found in groups, the most important of which are situated above the heart in the cephalothorax and at the rear limit of the abdominal segments. The movements of the white pigment are not very regular (p. 98), whereas the red and yellow pigments are expanded in light on a dark background but

concentrated in light on a white background and if the eyes are not stimulated by light (i.e. by night, in artificial darkness by day, or after covering the eyes with an opaque paint). Chloroform, ether, and extirpation of the eyes (Plate IX. 1) cause complete expansion of the chromatophores (Perkins, 1928). Covering the ventral half of the eyes with opaque paint ('ventral blinding') causes expansion of the red and yellow pigments in light independently of the colour of the background, whereas the same pigments after 'dorsal blinding' show the normal colour-change in light, i.e. contract the red and yellow chromatophores on a white and expand them on a dark background (Hanström, 1937). The same results are obtained if the animals are turned upside down after ventral or dorsal blinding. Thus if the ventral half of the eye of *Leander adspersus* is covered with an opaque paint and the normal position of the animal is reversed, the red and yellow pigments expand in light also on a white background (Hanström, 1938). Thus the decisive factor in the co-operation of the eyes with the nervous system and the endocrine organ during chromatophoral activity is the stimulation of the ventral half of the compound eye by light.

Besides the red, yellow, and white pigments there exists in *Palaemonetes* as in several other Decapods (especially shrimps) a blue diffuse pigment which is most easily observed when a black-adapted animal is transferred from a dark to a white background. In *Palaemonetes* it seems to be genetically related to the red pigment (Perkins, 1928; Brown, 1933–5; cf. Abramowitz, 1937, and this book, p. 96).

Brown (1935) investigated the response of *Palaemonetes* to variously coloured backgrounds, and obtained the same results on the whole as Koller in *Crangon*. Thus the red, yellow, white, and also the blue pigments concentrate and expand independently of one another, as the following scheme indicates:

Background	*Red*	*Yellow*	*White*	*Blue*
White . .	concentr.	concentr.	expand	absent
Green . .	concentr.	concentr.	expand	present
Red (1) . .	concentr.	expand	expand	absent
Red (2) . .	expand	expand	expand	absent
Blue . .	concentr.	concentr.	concentr.	present
Dark Grey .	expand	concentr.	concentr.	present
Black . .	expand	expand	concentr.	present

Brown concluded from these observations that different hormones regulate the concentration of the different pigments in *Palaemonetes*, but that their expansion is an innate function of the chromatophores. He further investigated the condition of the pigments after keeping the animals for several weeks on a background of a certain colour. In agreement with Megusar (1912) Brown found that the background response of the shrimps implies two factors: (1) the rapid movements of the pigment granules within the chromatophores, demanding 24 hours at most (the physiological colour-change); and (2) a variation of the quantitative amounts of the different pigments, depending upon a production of some and a destruction of others in accordance with a certain constant background colour—a slow process lasting several weeks (the morphological colour-change). At the same time Brown confirmed the view of Keeble & Gamble (1904), Babak (1913), Remane (1931), and Odiorne (1933) that the amounts of pigments which are kept constantly dispersed upon a given background increase simultaneously, whereas the amounts of pigments which are kept constantly concentrated on the same background decrease. Brown thinks therefore that it is possible that the same hormones which regulate the pigment migrations within the chromatophores (the physiological colour-change) are also active in the production and destruction of the pigments (the morphological colour-change). In his unpublished paper Carlson has remarked about this, that according to our present knowledge of this physiological phenomenon, no pigment-activating hormones should be present in the blood if the red and yellow pigments are dispersed in *Palaemonetes*, and thus the pigment-concentrating hormones from the eye-stalks of the Decapods cannot be supposed to act upon the morphological colour-change except perhaps as a negative factor whose absence permits the production of the pigments. Contrary to Brown's opinion it seems more probable to me that those hormones which concentrate the pigments would simultaneously act destructively upon them. This hypothesis may perhaps be favoured by the already mentioned production of the blue pigment from the red in *Palaemonetes*. This production takes place simultaneously with the concentration of the pigment, and probably implies a loss of substance of the red pigment.

With the extirpation of the eyes in the Decapoda Natantia (shrimps, prawns) most investigators have found a darker colour (Plate IX. 1) following the expansion of the red and yellow pigments (Parker, Brown, & Odiorne, 1935; Carlson, 1936). The sole exception has been *Hippolyte varians* according to Minkiewicz (1908). Dr. H. G. Welsh, however, who investigated this shrimp at the Marine Biological Laboratory at Plymouth in 1937, has informed me verbally that *Hippolyte varians* too, like other Natantia, expands its chromatophores after extirpation of the eyes. In his experiments Minkiewicz probably did not extirpate the whole eye. The Decapoda Brachyura (the crabs), however, of which *Uca pugilator* has been most thoroughly investigated, behave in quite another manner (Megusar, 1912; Carlson, 1935, 1936; Abramowitz, 1935). *Uca* has black (melanophores), red, yellow, and white pigments in its beautiful monochromatic chromatophores. After extirpation of the eyes *Uca* grows pale, since the black and red pigments concentrate (Plate VII), contrary to the conditions in the Natantia. In agreement with this, blinded animals according to Carlson (1935, 1936) grow darker after injection of their own eye-stalk extracts, the red and black pigments again expanding. Carlson (1936) further proved that extracts of the eye-stalks of *Uca pugilator*, injected into blinded and consequently dark or into dark-adapted *Palaemonetes vulgaris* and *Crangon* (*Crago*) *vulgaris*, cause a contraction of the black, red, and yellow pigments just as eye-stalk extracts of other Decapods. Eye-extracts of shrimps (*Palaemonetes*, *Crangon*) and other Decapods, injected into blinded and consequently pale *Uca*, always produce an expansion of the black and red pigments. Though other explanations are possible, it seems most simple to suppose that the same eye-stalk hormone (or hormones) which concentrates the red and yellow pigments in blinded *Palaemonetes* is the cause of the expansion of the black and red pigments in blinded *Uca*.

In his investigation of a number of Swedish Decapods Carlson has used a new technique for the study of the chromatophores of those species in which the chitin is especially thick or in which the pigment of the chromatophores is covered by pigments deposited in the cuticle itself. With a fine knife he has made 'windows' in the cuticle of the legs without damaging the hypodermis, and has thus been able to study the chromatophore

reactions in species which otherwise show no colour-change either macroscopically or microscopically (Plate VIII). The number of crabs which have been investigated for the common chromatophore reactions has thus increased, and it seems certain that all Decapoda Natantia behave on the whole like *Palaemonetes vulgaris*; that is, disperse their red and yellow pigments after removal of the eyes; and that all Brachyura behave principally like *Uca pugilator* i.e. concentrate their black and red pigments after this operation.

Kalmus (1938) has investigated a representative of the Reptantia Macrura, the common European crayfish, *Astacus vulgaris*. According to this investigation *Astacus* shows a periodical rhythm; the red and yellow chromatophores are concentrated by night and expanded by day. Blinding through removal of the eyes is followed by complete expansion of the red and yellow pigments as in the Natantia (and as was already observed by Megusar, 1912). Carlson has investigated *Homarus vulgaris* and *Nephrops norvegicus*, which also belong to the Reptantia Macrura, and especially the following members of the Reptantia Anomura: *Galathea squamifera*, *Munida bamffia*, *Gebiopsis* (*Upogebia*) *deltaura*, and *Eupagurus bernhardus*, which group had previously been hardly investigated at all in this respect. In all instances blinding was followed by an expansion of the red pigment, which is the chief or sole pigment of the chromatophores, and thus it seems probable that the Brachyura stand apart from all other Decapods in respect to their curious chromatophore regulation, which is contrary to that occurring in other members of the order. The Stomatopoda seem, however, to be in accordance, since *Squilla mantis* possesses brown and white chromatophores of which the brown according to Giesbrecht (1910) contract after extirpation of the eyes. Thus *Squilla* grows pale after blinding, whereas amputation of only one eye or of the distal part of the eye-stalks together with the eye does not cause contraction of the chromatophores. According to Giesbrecht, *Squilla* should not grow pale in darkness (by day), which is not surprising if it possesses a periodical colour-change and regularly expands its chromatophores by day.

Carlson has further shown that colour-change in the Brachyura generally agrees in most details with *Uca*. Thus the black and yellow pigments mostly or always behave in an opposite

manner. After blinding through extirpation of the eyes, the yellow pigment in the crabs is dispersed, just like the yellow pigment in the shrimps, perhaps because both may be carotinoids. As Abramowitz (1937) remarks, however, the chemistry of the pigments in the Crustacea is little known, and a comparison of the chromatophore reactions on a chemical basis is at present out of the question. The black chromatophores in *Ligia baudiniana* according to Kleinholz (1937) (cf. p. 116) probably contain melanin, but react oppositely to the melanophores in *Uca*, since after removal of the head they expand, and contract after an injection of extracts of the head. Abramowitz has further shown that no uniformity exists in the response of the various chromatophores in different Crustaceans with respect to the anatomical features of these organs, whether monochromatic or polychromatic. After analysing the reactions of the pigments of *Palaemonetes* on different backgrounds according to Brown (1935), Abramowitz refers to Brown's concept of the existence of one contracting hormone for each pigment: the 'multiple theory'. According to Abramowitz this theory requires the existence of a veritable array of hormones, and in contrast to it he presents a 'unitary theory'. The unitary theory aims at explaining the diversity of pigmentary reactions occurring among the Decapods equally well; according to it there is one common hormone whose effect on various integumentary pigments is determined by the chromatophoral organization of the species which decides the response to the hormone. This view has certain advantages in clarity but cannot explain why a particular pigment in one genus reacts in the opposite way to apparently the same pigment in another following the same surgical operation or following the injection of the same extract.

D. The Properties of the Pigment-activating Eye-stalk Hormone of Decapod Crustacea. The Connexion between Ca, Moulting, and the Function of the Chromatophores. The Physiology of the Pigment-activating Incretory Gland of the Eye-stalk. Perkins (1928) and Koller (1929, 1930) made the first statements concerning the physico-chemical nature of the pigment-activating hormone of Decapods. They have proved that this substance has a specific action, that it is conducted through the blood, is soluble in water, can be boiled without destruction, is neither species- nor group-specific, is still active after consider-

able dilution (at least 1 : 500,000), and is not spoiled by the action of the digestive enzymes. It can thus be administered *per os*. The eye-stalks can further be kept dry a long time, even a year (Hanström, 1937), and still give active extracts. Carlson (1936) has shown that the pigmentary hormone in *Palaemonetes* passes through a cellophane membrane, that it is not soluble in ether but soluble in alcohol, and that it is rather stable so that it can be boiled a short time with diluted HCl and NaOH without losing its activity.

Carlson calls special attention to the fact that these properties of the pigmentary hormone are not in accord with the view that the chromatophorotropic hormone is identical with the substance of the nature of the auxins which is said to have been detected in the eye-stalks of Crustaceans by Navez & Kropp (1934) and Kropp & Crozier (1934) (cf. p. 21). As Abramowitz (1937) writes, it would appear that these authors have not been dealing with the pigment-activating hormone but with another substance present in aqueous extracts of the eye-stalks of *Palaemonetes*. The interesting experiments by Navez, Kropp, and Crozier ought to be repeated and confirmed.

Finally, Abramowitz (1936, 1937) has tried to standardize the extract of the eye-stalks of *Uca pugilator* and purify it by means of the following method. One thousand eye-stalks of *Uca* were dried and pulverized. The total activity of the dry powder was 1,000 *Uca* units according to the standardization of Abramowitz, or 0·6 *Uca* units per mg. of dry powder. The material was extracted several times with small volumes of light petroleum ether in order to remove a red carotinoid pigment. The ether solution was washed with small amounts of distilled water. The water layer was then added to the residue insoluble in ether, and the ether layer being only slightly active was discarded. The residue which was insoluble in ether was then extracted three times with distilled water. The water solution was boiled and filtered and the filtrate dried in a current of warm air. The dried material was washed with small amounts of chloroform to remove traces of the red pigment, and the chloroform washings being only slightly active were discarded. The dried filtrate was then extracted with 95 per cent. ethanol, and the alcohol solution was centrifuged. The alcohol-soluble fraction was decanted and dried. Both the alcohol-soluble and

alcohol-insoluble fractions were active, the latter being much less so than the former, and hence it was discarded. The material soluble in 95 per cent. ethanol was then dissolved in hot absolute alcohol and precipitated by the addition of ether. The activity of the material soluble in absolute alcohol was approximately two *Uca* units per mg. The loss in total activity during these processes was about 60 per cent. The material soluble in absolute alcohol was devoid of pigment and apparently protein-free.

Abramowitz (1937) then ascribes to the hormone the following properties. The eye-stalk hormone is readily soluble in water, but not completely soluble in ethanol or methanol. It is only slightly soluble in acetone, and insoluble in organic solvents such as benzene, chloroform, or ether. The hormone is thermostable, but is destroyed by oxidation. It does not decompose when boiled with HCl or NaOH in a 1 per cent. solution for short periods of time. If the hormone is boiled for 2 hours with NaOH, the activity is completely destroyed. The hormone adsorbs easily on to various substances present in crude extracts of the eye-stalks. It may be kept in an aqueous solution in the refrigerator for some time without appreciable loss of activity, but is slowly destroyed when kept in an aqueous solution at room temperature.

It has already been mentioned (pp. 12, 25) that the Crustacean pigmentary hormone affects the chromatophores in vertebrates, and that the intermedin of vertebrates expands the chromatophores in such Crustaceans as *Uca* (which contracts the chromatophores after eye-extirpation). There exists, then, some evidence for an agreement in action and properties between intermedin and the pigmentary hormone in Decapods, but of course there are several and perhaps more important differences. In shrimps (*Leander adspersus*) I (1937) was, however, unable to find any expanding action of intermedin upon the chromatophores; if this hormone really had any action (which is very uncertain) it was a weak contraction. This result is not impossible to explain, since the chromatophores in crabs (*Uca*) and shrimps (*Leander*) behave in an opposite manner. Now in the frog, intermedin and adrenaline act antagonistically, the former substance expanding, the latter contracting the chromatophores. It is true that Kalmus (1938) did not observe any action of

adrenaline on the chromatophores of *Astacus fluviatilis* (whose chromatophore reactions belong to the same type as those in *Leander*), but Beauvallet & Veil (1934) state that they have been able to expand the chromatophores in *Leander* (*Palaemon*) *squilla* with adrenaline, and to contract them repeatedly with eye-stalk extracts and again expand them with adrenaline in the same animal. Thus the eye-stalk extract of *Leander squilla* in this instance acts antagonistically to adrenaline, which fact lends some support to the physiological comparison between the common Crustacean eye-stalk hormone and intermedin. It seems that a comparative study of the action of intermedin, adrenaline, and the Crustacean chromatophorotropic hormone upon the chromatophores in a crab and a shrimp would advance our knowledge of the properties of the last-named hormone considerably.

The migration of the pigment granules within the chromatophores of Crustacea is, when fully developed, one of the most beautiful and rapid biological reactions which can be observed in nature or in the laboratory. Koller (1937) says: 'The centrifugal and centripetal streamings of the granules and the condition of dispersal of the different pigments can be read off as the column of liquid in a manometer, especially when using the method of observation elaborated by Perkins-Snook (1931).' Koller (1930) has also tried with Crustacean material to solve the question how the hormones act upon the animal chromatophores.

The chromatophores of Crustacea are surrounded by a membrane, and the migration of the pigment granules takes place within the branches of the chromatophores, being caused by protoplasmic streamings. The elastic chromatophore membrane is permeable, and the streaming of the pigment granules is retarded in a hypertonic medium (in *Crangon*) probably because the increased salinity deprives the chromatophores of water. On the other hand, in a hypotonic medium the content of the chromatophores is diluted through absorption of water and the movements of the granules become more rapid. The experiments of Koller further proved that the Ca-ions of sea-water are of special importance for the pigmentary reactions. If *Crangon* is kept in Ca-free, though isotonic sea-water, it loses the power of concentrating the melanin. Animals which have been kept

on a black background in water devoid of Ca for some hours remain dark during several days even if kept on a white background. It may be supposed that the changes which are observed in Ca-free water are due to a disturbance of the properties of the chromatophore membrane, and it seems probable that the colour-change hormones exercise their influence upon the permeability of the chromatophore membranes, and thus also upon the pigment migrations, by means of the Ca-ions (Koller, 1930).

It may be of interest in this connexion to call attention to the fact that adrenaline increases the viscosity of the protoplasm and retards the protoplasmic streamings in the Protozoa (Bauer, 1926; von der Wense, 1935; cf. p. 13). Von der Wense (1934, 1935) has further shown that the action of adrenaline is dependent upon the Ca-content of the surrounding medium; if the surrounding water is devoid of Ca the adrenaline has no effect. The adrenaline seems to increase the Ca-content of the protoplasm and thus cause the increased viscosity.

In discussing the finer mechanism of the pigment migrations, it is of importance to know which ought to be regarded as the state of rest and which the state of activity of chromatophores. According to Parker (1935), in the melanophores of fishes (*Fundulus*) neither the state of concentrated pigment nor that of dispersed pigment nor any intermediate condition is necessarily a state of rest. If the terms rest and activity are to be used for chromatophores, rest is a state of quiescence of the melanin particles, and activity their motion. Such a state of activity can be shown to be associated with much Brownian movement among the pigment granules and the state of rest with very little of this movement; which fact according to Parker suggests that in the state of activity the melanophore protoplasm has the character of a sol and in that of rest the character of a gel.

Koller (1930) has found a probable connexion between the hormone-producing organ of the eye-stalk in *Crangon* and the Ca-metabolism, and regards this as a factor in favour of his hypothesis of the importance of Ca for the chromatophore functions. Though Koller extirpated a region of the eye-stalk which was supposed to contain the 'white-organ' of *Crangon*, he probably simultaneously extirpated the sinus gland, the real source of the pigment-activating hormone in the Decapods. In

a number of animals in which this region of the eye-stalk had been cauterized the moulted skins were dried and weighed after each moult and compared with normal animals. It was found that the skin weight of normal animals was always higher than in the operated ones and that the higher weight was due to a higher content of Ca in the former, the chitin weight being the same in both series. In this connexion it may be added that the biochemistry of moulting has been investigated by Drilhon (1935) in *Maia squinado* and the Ca-metabolism by Robertson (1938) in *Carcinus maenas*. Of special interest is the investigation by Plankemann (1935) on moulting in *Crangon vulgaris*, *Leander adspersus*, and *Leander squilla*, from which it was found that the amount of chitin in the skin of starving animals is increased and that the moults are retarded in sea-water containing high amounts of Ca, but are not retarded in water containing less than normal amounts of Ca. Plankemann believes that the rhythm of moulting is determined by the carbohydrate metabolism and is caused by hormones, which sounds very probable, especially if compared with the conditions in insects (p. 58).

An interesting fact which also seems to be in favour of the theory of a connexion between the incretory organ of the eye-stalk and moulting is the observation that after the extirpation of the eyes in the Decapods at least the first moult takes place at an earlier date than in normal animals. I have observed this fact repeatedly at the moulting of young *Eriocheir sinensis* during an investigation in 1937 which is not published, and have found the same observation in the paper of Megusar (1912). According to Megusar not only the first but also the subsequent moults take place much earlier in blinded *Astacus vulgaris* than in normal. According to these observations it would seem as if the incretory organ of the eye-stalk which is extirpated together with the eye-stalk itself and is perhaps functionally connected with moulting (the sinus gland?) acts by retarding the shedding of the cuticle, since in its absence the moult takes place earlier than normally. Now if the hormone acting on moults and retarding them is identical with the pigment-concentrating hormone acting on the colour-change, this would agree with the fact that according to Plankemann (1935) the moults are retarded in water with a high content of Ca. Such water does not interfere with the action of the pigment-activating hormone,

whereas water containing little or no Ca does not retard the moults but, according to Koller (1930), expands the chromatophores in *Crangon* (p. 109) and thus prevents the action of the pigmentary hormone. It may be added that in an organ of *Oniscus murarius* which probably corresponds to the sinus gland in the Decapoda (p. 89), Walker (1935) has found certain concretions probably consisting of calcium phosphate according to their chemical properties. This observation may be of importance in connexion with an investigation of the chemical properties and the more detailed function of the secretion of the sinus gland. In the sinus gland of *Uca* and other crabs I have also noted the presence of concretions which may be identical with those described by Walker.

The problem of a connexion between colour-change, moulting, and the content of Ca in the surrounding water may at present be summed up in the following manner. Extirpation of the eye-stalks is followed by precocious moulting. Thus it seems possible that an organ in the eye-stalks retards the moults by means of a hormone. The moults are also retarded in water with a high content of Ca, which thus increases the action of the moulting-retarding eye-stalk hormone. Such water does not prevent the action of the pigment-concentrating hormone, but water with little or no Ca does not retard the moults and expands the chromatophores, thus decreasing the action of the moulting-retarding hormone and likewise decreasing or preventing the action of the pigmentary hormone. These substances would then both have their source in the eye-stalks and some other properties in common, so that it seems possible that they may be identical. Now if the secretion of the incretory eye-stalk organ acts upon the Ca-content of the body in a certain way or if it itself contains Ca (since the organ in *Oniscus* possesses concretions of a Ca-compound), its action may be supposed to correspond to the action of Ca in the surrounding water upon colour-change and moulting, i.e. the supply of Ca to the integument retards the moults and also retards the protoplasmic streaming and the pigment migration in the chromatophores, concentrating the pigment granules. After eye-extirpation and the simultaneous extirpation of the incretory organ, the chromatophores are expanded and the rate of moulting increased.

I need not point out that this account of the connexion between colour-change and moulting is purely hypothetical and that, if later confirmed, it can only be valid for most Decapods, and not in details for the Brachyura in which eye-extirpation is followed by a contraction of the chromatophores. If there really is a connexion between the pigmentary hormone and the moulting there may also be a connexion between the former and metabolism as was proposed by Menke (1911). Thus according to Mollitor (1937), the moults are, in a certain degree, connected with the excretory activity of the hypodermis; Keeble & Gamble (1905) have discussed the possibility of a connexion between fat metabolism and the function of the chromatophores, and Koller (1936) has made it probable that the blue pigment (pp. 96 and 103) constitutes an intermediate stage of the metabolism and has something to do with the fats.

Following on certain experiments by Kropp & Crozier (1934) (cf. p. 21), I made (1937) some experiments to see if the content of the pigment-activating hormone in the eye-stalks was the same in animals kept for some time in darkness as in animals kept for some time in light. I did not get any conclusive evidence in this respect in the crabs *Carcinus maenas* and *Callinectes sapidus*, but later experiments by Abramowitz (1937) with a more elaborate technique showed that in the shrimp *Palaemonetes* (but not in the crab *Uca*) the amount of the pigmentary hormone in the eye-stalks of animals kept in total darkness is about half that which is found in normally black-, white-, yellow-, and blue-adapted animals kept in light. It is especially interesting that the amount of hormone found in the eye-stalks of black-adapted animals is about the same as that found in white-adapted. In the latter there must be a continual release of the hormone into circulation, in the former none, or only a subminimal release. Abramowitz believes, however, that the red chromatophores in *Palaemonetes* maintained in darkness are expanded, and thus that there ought not to be any release of the pigmentary hormone into the circulation in these circumstances (by night or in artificial darkness). Though Brown (1935) is of the opinion that the red pigment is dispersed in darkness, he himself (1933) has confirmed the statement of Perkins (1928) that the said pigment is concentrated in darkness, a position of the red pigment which

1 (1937) always found in *Palaemonetes* during night experiments or in animals kept in artificial darkness by day. According to this fact there must also be a release of the pigmentary hormone into the circulation in darkness in agreement with what I wrote in 1937: 'The pigment-concentrating hormone of *Palaemonetes vulgaris* is continuously released under normal conditions; only if the ventral half of the eye is stimulated by the reflected light from a dark background is the release of the hormone inhibited.' But as the amount of hormone found in the eye-stalks of white-adapted animals kept in light (in which the chromatophores are contracted and a release of the hormone is obvious) is twice that obtained from animals maintained in darkness (in which, according to Perkins and my own observations, the chromatophores are contracted), the conclusions of Abramowitz (1937) regarding the necessity of light for the synthesis of the hormone are probably correct. 'Regardless of background', Abramowitz writes, 'light causes an acceleration in hormone synthesis, and light impinging on certain backgrounds such as white, causes a maximal release of the hormone into circulation with a concomitant increase in rate of production of the hormone.'

Uca, as a representative of the Brachyura, undergoes a periodic change in colour (as do certain other Crustaceans, e.g. *Leander squilla*, and, further, *Astacus fluviatilis*; cf. pp. 93 and 105) and the background adaption is lacking (Megusar, 1912; Carlson, 1935, 1936; Abramowitz, 1936, 1937). The animals are dark by day and pale by night (according to Carlson all investigated Swedish crabs contract their melanophores by night), and this cycle repeats itself regardless of background or light-intensity. When the eye-stalks and their incretory organ are removed, the rhythm is permanently abolished and the animals remain pale (p. 104). In *Uca* (and other *Brachyura*; p. 105) the pigmentary hormone expands the black and red chromatophores and thus by night there is no release of the hormone. According to Abramowitz the amount of hormone present in the eye-stalks is the same whether the animals are in the pale or in the dark phase of their rhythm. Then both release and synthesis of the hormone in *Uca* ought to be independent of environmental conditions, and controlled by a diurnal discharge of impulses from the nervous centre of the hormone gland. The discharge during daytime would bring

about a 12-hour release of the hormone with a concomitant increased rate of production; the absence of the discharge during the night would cut off the release and slow down the rate of synthesis.

E. **The Distribution of the Chromatophorotropic Hormone among the Crustacea.** While the occurrence of pigmentary hormones in the Decapoda has been so extensively investigated that there is little doubt that all Decapod Crustacea possess them, the other orders of the class have not been at all satisfactorily examined in this respect. These, especially the Entomostraca, are also commonly much smaller and they mostly have sessile, not stalked, eyes; thus it is necessary to make extracts of the whole heads instead of the eyes. Further, the small body-size often makes it impossible to inject the extracts into the same species, so that the presence or absence of pigmentary hormones must be investigated by injecting the extracts into the larger Decapod Crustacea.

According to Ståhl (1938) the lowest members of the Crustacean group, the *Phyllopoda*, also seem to be equipped with pigmentary hormones. Thus in the extracts of the heads of *Artemia salina* Ståhl found a substance which gave an obvious, though weak, contraction of the chromatophores in blinded *Leander adspersus*. The Phyllopoda seem only rarely to possess chromatophores, and a colour-change has not been described in members of this order. In *Artemia salina*, however, the colour is unusually variable and also very beautiful, but it is not due to chromatophores. On the other hand, well-developed chromatophores are found in some Cladocera; for instance, *Latona setifera* (Weissmann, 1879; cf. Brehm, 1938). In some other members of the Entomostraca, i.e. in the Copepoda Harpacticidae, well-developed chromatophores have been detected. Thus Lang, in an investigation (not yet published), has found chromatophores in the rock-pool harpacticid *Tigriopis fulvis*. Head extracts of a species of the Cumacea, *Diastylis rhatkei*, also concentrated the expanded red and yellow pigments in blinded *Leander adspersus* (Ståhl, 1938).

The occurrence of pigmentary hormones in the Isopoda has been investigated by Kleinholz (1937), Ståhl (1938), and Smith (1938). Ståhl examined the terrestrial Isopods *Oniscus murarius* and *Porcellio scaber*, *Idothea baltica* from brackish water in the

Sound (Öresund), and *Mesidothea entomon* from the brackish water of the Baltic. The extracts of *Oniscus*, *Porcellio*, and *Mesidothea* gave a surprising result; injected into blinded *Leander adspersus* with maximally expanded chromatophores no reaction was observed, whereas an injection into white-adapted *Leander* caused an obvious though weak expansion of the contracted chromatophores. To achieve any results Ståhl had to use rather strong extracts, and thus he regards the reactions as not necessarily hormonal. Extracts of *Idothea baltica*, finally, did not yield any conclusive evidence but probably caused a weak concentration of the red and yellow pigments in blinded *Leander adspersus*. It is interesting to note that of these four Isopods which seem to be devoid of the common pigmentary hormone of the Crustaceans (which concentrates the expanded chromatophores in shrimps) two are terrestrial, whereas two occur in brackish water.

In the marine Isopod *Ligia baudiniana*, Kleinholz (1937) has found a pigment-activating substance which, though not yet tested on the chromatophores of Decapods, seems more to agree with that of these Crustaceans than that occurring in the head of *Oniscus*, *Porcellio*, and *Mesidothea*. *Ligia* shows a diurnal rhythm, being dark by day and pale by night—also in constant artificial darkness. Specimens of *Ligia* which were blinded through removal of the eyes with a needle or by covering them with an opaque mass grew darker or dispersed their pigments maximally. Those specimens whose eyes had been covered grew pale again by night. Injections of aqueous extracts of the heads into the body-space of dark *Ligia* brought about lightening by a concentration of the melanophores, as in the shrimps (p. 104). Hence Kleinholz concludes that the diurnal pigmentary activity is not due to a cycle of exhaustion and elaboration of secretory material in the endocrine gland controlling the colour-change.

Smith (1938) examined the colour-change of the related species *Ligia oceanica* without making any injection experiments, but using a method formerly applied to the investigation of the chromatophores in vertebrates (cf. Hogben & Slome, 1936). According to Smith, *Ligia oceanica* has melanophores and xanthophores, of which the former are the chief agents of visible colour-change. This consists in an expansion of the melanophores on a black background, and a concentration of them on

white by day. Animals blinded by painting over the eyes with black enamel show a stage of melanophore expansion less than in seeing animals on a black background, and considerably more than in non-blinded animals on a white background. In darkness the melanophores assume an intermediate condition and are less expanded than in blinded animals in light. Smith studied 'the time relations of chromatic function', i.e., the time necessary for the chromatophores to contract or expand when the background is reversed from white to black and vice versa, and the equilibrium intervals for transition from illumination on a white and black background to darkness and vice versa. According to Smith these time relations show that the background response is controlled by two hormones, one concentrating and one expanding. He also studied the relation of the different parts of the eyes to the chromatophoral activity, and distinguishes two groups of ocelli. One dorsal group is accessible to direct overhead illumination and is responsible for initiating the discharge of the hormone which brings about melanophore expansion. The other lateroventral group picks up light reflected from the immediate surroundings and is responsible for initiating the discharge of the hormone which evokes melanophore contraction. These observations are of interest when compared with my own investigations of the relation between the chromatophore reactions and the function of the different parts of the eyes in *Palaemonetes vulgaris* (1937) and *Leander adspersus* (1938), and ought also to be compared with the results of Ståhl in *Oniscus*, *Porcellio*, and *Mesidothea*. It seems, further, that the difference between the chromatophore activity in *Ligia baudiniana*, investigated by Kleinholz, and *Ligia oceanica* calls for further studies.

Representatives of the Amphipoda have been investigated for the occurrence of colour-change hormones by Koller (1936) and Ståhl (1938). The latter made extracts of the heads of *Gammarus locusta* which gave a rapid and strong contraction of the expanded red and yellow pigments in blinded *Leander adspersus*. Thus this substance shows the normal reaction of the Crustacean pigmentary hormone. Koller examined *Hyperia galba*, which species lives pelagically, attached to medusae of the species *Cyanea capillata*. Whereas free-swimming individuals show expanded chromatophores (according to Koller probably

melanophores) the chromatophores in attached *Hyperia* are contracted (cf. Lehmann, 1923). From his experiments Koller concludes that the contraction of the chromatophores in attached animals is the result of a lower general metabolism, the expansion in free-swimming animals a consequence of a higher rate of metabolism. Extracts of the head of *Hyperia* injected into other specimens expanded the melanophores. In this respect *Hyperia* seems to agree with the Brachyura, which expand their melanophores after injection of an extract of their own eye-stalks. Extracts of the eye-stalks of *Carcinus maenas*, injected into *Hyperia* with half-expanded chromatophores, gave, however, a further contraction, which does not agree with the view that the pigmentary hormones in *Hyperia* and Decapods are identical. Further investigations are necessary to clarify the relation between the two hormones.

The distribution of pigmentary hormones in the Mysidacea was investigated by Koller & Meyer (1930), Kropp & Perkins (1933), and Hanström (1937). Koller & Meyer studied *Praunus* (*Macromysis*) *inermis* and *Praunus flexuosus*, and Kropp & Perkins *Mysis stenolepis*. The eye-extracts of *Praunus inermis* and *Mysis stenolepis* had the same influence upon the melanin in *Crangon* as the Decapod eye-extracts, whereas, according to Koller & Meyer, extracts of white-adapted animals of *Praunus flexuosus* expand the melanophores in *Crangon*; extracts of black-adapted *Praunus flexuosus* are said to have no influence at all. I repeated the experiments with extracts of the eye-stalks plus the head of *Praunus flexuosus* which were injected into blinded *Leander adspersus*. In this instance I obtained the same contraction of the expanded red and yellow pigments as with extracts of the Decapod eyes, and extracts of *Praunus flexuosus*, injected in white-adapted *Leander*, yielded no conclusive evidence. It seems as if the pigmentary hormones in the Decapoda and the Mysidacea thus far investigated are the same, and all concentrate the expanded red and yellow pigments in Decapoda Natantia.

According to experiments by Carlson, not yet published, the Euphausiacea (*Meganyctiphanes norvegica*) also possess a pigmentary hormone which contracts the expanded chromatophores in blinded *Leander adspersus*. In the Stomatopoda (*Chloridella empusa*) I found (1937) a hormone which expands the concentrated black and red chromatophores in blinded *Uca pugilator*.

In both instances the reactions are the same as for the common Decapod pigmentary hormone. The chromatophore reactions of another species of the Stomatopoda, *Squilla mantis*, are reviewed on p. 105 in the light of Giesbrecht's (1910) work. It is of special interest that the brown chromatophores in *Squilla* contract after eye-extirpation, this being the same reaction as is found in the Decapoda Brachyura. These two groups are the only Crustaceans known with certainty to react in this manner, though the chromatophores in *Idothea tricuspidata* are said to expand after injection of eye-extracts of *Crangon vulgaris*, *Praunus inermis*, and *Praunus flexuosus* (Koller & Meyer, 1930). *Hyperia*, in agreement with the condition in the Brachyura, expands the melanophores after injection of its own extracts, but contracts them after injection of *Carcinus*-extracts (Koller, 1936).

In each order of Crustacea except the Decapoda only a few species have been investigated for the occurrence of the chromatophorotropic hormone. But as far as our present knowledge goes, it seems as if all orders of higher stalk-eyed Crustacea, the Mysidacea, Euphausiacea, Stomatopoda, and Decapoda, possess the same pigmentary hormone, which is normally produced in the eye-stalks. In other orders of Crustacea, the Phyllopoda, Cumacea, Isopoda, and Amphipoda, of which the latter three are sessile-eyed, the investigations have so far yielded very confusing results and call for further comparative studies. The Cumacea (*Diastylis rhatkei*) seem to agree with the conditions in the higher stalk-eyed groups. Since the next chapter shows that the sinus gland is probably the source of the chromatophorotropic hormone in the Decapoda, it is interesting to note that a sinus gland of a structure in all instances referable to a common type is found in all stalk-eyed higher Crustacea (Mysidacea, Euphausiacea, Decapoda, Stomatopoda), and that a small organ of the same kind is also detected in the Amphipoda and Isopoda (pp. 89 and 90). The Phyllopoda and Cumacea have still not been investigated satisfactorily in this respect.

F. The Localization of the Source of the Chromatophorotropic Hormone in Decapod Crustacea. Perkins (1928) proved that in the eye-stalks of *Palaemonetes vulgaris* one or more substances are produced which are able to concentrate the red and yellow pigments of the body chromatophores, and Brown (1935) found that a substance with the same properties can also be

extracted from the ventral ganglia, in which, however, it occurs in a much weaker concentration. In addition, Brown extracted substances both from the eye-stalks and from the anterior portion of the cephalothorax which concentrate the white chromatophores. After the detection of the general occurrence of the common chromatophorotropic hormone in the eye-stalks of Decapods, Koller (1930) and Hosoi (1934) made the first attempts at a more exact localization of the source of the pigmentary hormone within the eye-stalks of *Crangon vulgaris* and *Penaeus japonicus*. Both found that extracts of the distal part of the eye-stalk, which chiefly consists of the eye proper, have no influence on the chromatophores. According to Hosoi, the source of the pigmentary hormone is situated in the middle portion of the eye-stalk, whereas Koller after cauterization concluded that a certain organ, 'die Blutbildungszellen mit grossen Kernen' in the neighbourhood of the basement membrane of the eye, is the incretory organ sought after. As the present writer (1935, 1937) and Carlson (1935, 1936) have shown, it seems certain that the sinus gland (or blood-gland) which I discovered in 1933 produces the hormone (or hormones) which concentrate the red and yellow pigments in *Palaemonetes vulgaris* and expand the black and red pigments in *Uca pugilator*.

If one eye-stalk is completely extirpated in *Palaemonetes* and then the distal third of the other eye-stalk, containing the eye proper (cf. Plate X), is amputated, white-adapted animals remain pale (at least for some time), whereas in black-adapted animals the chromatophores are concentrated (Hanström, 1937). If, on the other hand, one eye-stalk is completely extirpated and on the other side the distal two-thirds are amputated, the chromatophores are completely expanded as in animals quite devoid of eye-stalks. In agreement with these observations, extracts of the distal thirds of the eye-stalks of *Palaemonetes* have no influence on the pigment migrations, whereas extracts of the distal two-thirds act as strongly as extracts of the whole eye-stalks. In *Palaemonetes* also the active gland must be situated in the middle third of the eye-stalk.

Also situated in the middle third of the eye-stalk is the organ which produces the hormone which in *Uca* (and other crabs) expands the black and red chromatophores. In *Uca*, Carlson (1935, 1936) completely extirpated one eye on one side and

the distal third of the eye-stalk on the other without any consequence for the colour-change in dark animals (the experiment was made by day, when *Uca* is dark; cf. p. 114). If, further, the next (the middle) third of the eye-stalk was extirpated, dark animals grew pale through concentration of the black and red pigments and remained constantly pale as if both eye-stalks had been completely extirpated (Plate VII). Within the middle third of the eye-stalk there exist in *Palaemonetes* both the sinus gland and the X-organ (Plate X) which I described as an incretory organ in 1931, whereas in *Uca* the middle third only contains a well-developed sinus gland and probably no X-organ at all. This supports the theory that the sinus gland produces the common chromatophorotropic organ of the Decapods. Through similar localization experiments in a number of American Decapods I was able to show (1937) that the source of the pigmentary hormone could always be traced to the place in the body containing the sinus gland. If, as in *Homarus americanus* and *Pagurus pollicaris*, this organ is situated in the proximal half or the two proximal thirds of the eye-stalk, the extracts of these portions are active (Plate IX). In *Callinectes sapidus* and *Ovalipes ocellatus* the distal half of the eye-stalk gives rise to an active extract, the proximal to an inactive; the former contains the sinus gland. Finally, in certain Anomura with more or less reduced eyes the sinus gland is situated in the head and not in the eye-stalks. In these instances (*Hippa talpoida*, *Gebia affinis*) extracts of the eye-stalks do not act upon the chromatophores, whereas the heads (the anterior portion of the cephalothorax) give rise to an extract which concentrates the red and yellow pigments in *Palaemonetes vulgaris* and expands the black and red pigments in *Uca pugilator*. Finally, the sinus gland is a constant feature in the Decapod Crustacea, whereas the X-organ (which is commonly situated in the neighbourhood of the sinus gland) is sometimes wanting. Thus I was not able to detect any X-organ in *Cambarus*, *Astacus vulgaris*, *Sesarma cinereum*, and *Aratus pisoni*, and yet extracts of their eye-stalks acted strongly upon the chromatophores. Since no other structures in the eye-stalks could be supposed to function as incretory organs, it seems unquestionable that the sinus gland is the source of the common chromatophorotropic hormone in the Decapod Crustacea.

XI

HORMONAL REGULATION OF THE RETINAL PIGMENT-MIGRATION IN CRUSTACEA

A. **Eye-stalk Hormone and Retinal Pigment Migration.** During my investigations of the endocrine organs and the hormones of the eye-stalks in Crustacea, I found that the sinus gland exists in Decapods living under the most different conditions. Thus I have found it in littoral species like *Palaemonetes vulgaris*, in pelagic species living at the surface like the sargassum shrimps *Leander tenuicornis* and *Latreutes fucorum*, in deep-sea species like *Acanthephyra purpurea*, in marine, brackish water, and fresh-water species (*Cambarus*, *Astacus*, *Macrobrachium*), in seeing and blind species (*Lepidopa*, *Eryoneicus*), in species without any macroscopically manifest colour-change (*Homarus americanus*, *Hippa talpoida*, *Libinia dubia*, *Cancer irroratus*), and species quite devoid of chromatophores (*Anchistioides antiguensis*). By injection experiments it was proved that the common chromatophorotropic hormone was also present in such forms as *Homarus*, *Hippa*, *Libinia*, and *Cancer*, in which the sinus gland shows every sign of a vigorous secretory activity. In *Anchistioides*, too, which has no chromatophores at all, the sinus gland is of a normal structure. Though Carlson in his unpublished paper has also detected functional chromatophores in species in which the chromatophores are covered by a thick cuticle and there is no obvious colour-change (Plate VIII), it seems probable that on account of its universal distribution in the Decapods the sinus gland has other and perhaps more important functions besides the regulation of colour-change.

One more hormonally regulated function can be traced to the eye-stalk in Decapods, namely the pigment-migrations of the compound eye, through which it adapts itself to light and darkness. The compound eye in Decapods often possesses three different kinds of pigment cell which perform partly independent characteristic migrations in light and darkness. The first to describe the pigment adaptation in a compound eye was Exner (1889) in insects; he also (1891) dealt extensively with the physiology of the compound eye in insects and Crustacea. Parker (1897) was, however, the first to give a detailed account

of the pigment-migration in the compound eye of Crustaceans. In this paper he tried to analyse the nature of the pigmentary movements of the three different pigment-cells in the eye of *Palaemonetes vulgaris*. Owing to this and subsequent investigations, *Palaemonetes vulgaris* is the shrimp which has been most thoroughly examined in respect to both its colour-change and the anatomy and physiology of its compound eyes (Plate X).

The ocelli of the compound eye of *Palaemonetes* (Plate X, Fig. 17) according to Parker (1891, 1897) and Welsh (1930, 1932) contain: (1) quadrangular corneal lenses which are secreted by two underlying hypodermis cells; (2) the crystalline cone (the dioptric system), built up of four cone-cells, the nuclei of which have a distal position; and (3) the rhabdome (the receptive element), which is made by fusion of the inner differentiated faces of eight retinular (visual) cells, one of them being rudimentary. The crystalline cones are surrounded in sleeve-like fashion by two distal or iris pigment-cells. The distal portions of these reach as far as the cornea, and the proximal portions seem to be continuous with the retinular cells. The retinular cells are also pigmented, and thus are called proximal pigment-cells by the American investigators. Their nuclei are situated at the same level as the proximal ends of the cone-cells, and their nerve-fibres, one for each functional retinular cell, pass proximally through perforations in the basement membrane and terminate in the first optic ganglion, the lamina ganglionaris (Plate X). The third kind of pigment-cell is the reflecting pigment- or tapetum-cells which are situated in the proximity of the basement membrane and are capable of moving outwards to the front face of the distal pigment-cells and inwards along the retinal nerve-fibres as far as the lamina ganglionaris. Probably there are only one or two reflecting pigment-cells in each ocellus (ommatidium).

The pigment of the distal and of the proximal pigment-cells is black and consists of melanin (Parker 1932). The reflecting pigment is white, at least when viewed by reflected light, and is made up of guanin (Welsh, 1932). Since the white integumentary chromatophores at least in *Eriocheir sinensis* are composed of uric acid (Mollitor, 1937), which like guanin belongs to the purine derivatives, it would be interesting to investigate in a crab whether there is any connexion between the

migration of the melanin in the eye and that of the integumentary melanophores on the one hand, the guanin in the eye and the white integumentary chromatophores on the other.

The function of the distal or iris pigment-cells is the best known of the three different pigment-cells in the eye of *Palaemonetes*. In bright light the distal pigment is proximal in position and borders upon the pigment of the retinular cells; in darkness it is more distally located between the cones. In the first instance the eye is supposed to function as an apposition eye, in the second as a superposition eye (Exner, 1891). In this manner the amount of light reaching the rhabdomes is sharply limited in bright light, whereas in dim light the pigment sheaths allow most of the light available to reach the sensitive rhabdomes through numerous avenues. Thus the migration of the distal pigment adapts the eye for seeing by day and night.

The movements of the distal pigment-cells are brought about in two different manners in different Decapods. Thus in some species, like *Palaemonetes* and *Palaemon*, the cells form a sheath around the cone and rhabdome of the ommatidium and slip as a whole up and down this axis (Fig. 17). The second type of migration is represented by, e.g., *Astacus*, *Cambarus*, and *Pagurus*. In these the cell-bodies remain essentially motionless at the level of the cones, and instead their pigment-granules move inwards into the proximal processes of the cells and back again to the bodies of the cells. The function of the iris pigment-cells of the first type was suggested by Parker (1897) to be the result of combined amoeboid and muscular movements, by Trojan (1913) and Mossler (1915) to be akin to protoplasmic streaming. Welsh (1930) noticed that each of the two distal pigment-cells contains in its interior 3–4 fibrils which extend from the distal end of the cell-body to the end of the proximal process, where they terminate at the level of the nuclei of the retinular cells (Fig. 17). The fibrils are thus as numerous as the retinular cells, viz. 7–8. When the distal pigment-cells migrate inwards under the influence of light, these fibres shorten to one-fourth or one-fifth of their former length and thicken correspondingly. Welsh therefore supposes them to be myofibrils and in the main responsible for the proximal movement of the distal pigment-cells. The outward migration of the same cells in darkness cannot be explained in the same manner, for the distal processes

are not known to contain any such fibrils. The mechanism of this migration is also still unknown, but according to Parker (1932) some kind of primitive muscle-like or amoeboid action may take place within the distally elongated processes of the distal pigment-cells.

The second type of migration of the distal pigment-cells is distinguished by what is usually assumed to be the result of protoplasmic streaming of the pigment-granules. The cell-bodies themselves remain completely or almost completely motionless at the level of the cones, but the granules move inwards into the long proximal processes of the cells under the influence of light, and back again into the cell-bodies under the influence of darkness.

The retinular pigment-cells surround the rhabdome, and their pigment-granules move outwards under the influence of light so that they completely fill the retinular cells from their fibrous extensions below the basement membrane to the nucleated distal portions. Under the influence of darkness the granules migrate inwards and are usually limited to the fibrous elongations of the retinular cells below the basement membrane. The consequence is that the pigments of the distal and proximal pigment-cells approach one another in the light and separate in the dark (Fig. 18). The pigment of the retinular cells is believed to control the amount of light that falls upon the rhabdome, which function is carried out in connexion with the reflecting pigment.

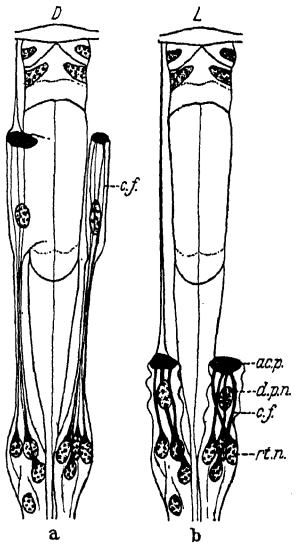


FIG. 17. Longitudinal sections of ommatidia from depigmented eyes of *Palaemonetes vulgaris*, showing the contractile fibrils which are found in the distal pigment-cells. *a* from dark eye showing fibrils in a relaxed condition; *b* from a light eye showing fibrils in a contracted condition; *ac.p.* accessory pigment; *c.f.* contractile fibril; *d.p.n.* nucleus of distal pigment-cell; *rt.n.* nucleus of retinular cell. After Welsh.

The movement of the reflecting pigment is said by Welsh (1932) to be in part of the amoeboid type, in part performed

by means of protoplasmic streamings. In light the pigment-granules are chiefly found proximally to the basement membrane, in darkness chiefly on the distal side of it (Fig. 18). The inward migration of the retinular pigment in the dark exposes the reflecting pigment in such a way that light which has already passed once through the rhabdome from the outside may be reflected again in order to multiply the action.

It is obvious that the migrations of the eye-pigments are influenced by light, but whether this effect is a direct action of light upon the pigment-cells or not was for a long time an open question. It is equally probable that the light stimulates a receptor which in its turn induces changes which spread to the pigment. In this instance the migrations of the eye-pigments would represent the final stage in a reflex-circuit.

If the eye-pigments are directly sensitive to light and are not stimulated simultaneously by other means or through the nervous system, the condition of the pigments in a light-adapted eye of an animal should have no influence on the pigments of the other eye of the same animal if this is covered by an opaque paint. Conversely, if the nervous system is involved in the pigment-migration, one eye may be influenced by the condition of the other. Parker (1897) and Castle (1927), who studied the migration of the eye-pigments in *Palaemonetes*, concluded that the illuminated eye was without effect on the position of the pigments in the covered eye, and that retinal pigment-migration was independent of the central nervous system. Demoll (1910, 1911, 1917), Trojan (1913), and Bennit (1924) believed, however, in the nervous control of pigment-migration in the compound eyes, and von Frisch (1908) was unable to get any conclusive evidence from his experiments on insects and Crustacea. The fact that the histologists have not succeeded in finding any nerve-endings within the compound eye does not favour the view that the migration of the eye-pigments is regulated by the nervous system.

Of great interest in this connexion is the fact, observed comparatively recently, that the eye-pigments in several Crustaceans show a diurnal movement like that occurring in the chromatophores in some species (p. 114). Thus Welsh (1930) found that the distal pigment in *Macrobrachium* by day assumes the position characteristic for light-adaptation and by night

that characteristic for dark-adaptation, independently of the intensity of light. In an animal fully illuminated from a 100-watt lamp the distal pigment at about 6 p.m. will begin to migrate outwards as if the animal was kept in darkness, and if kept in darkness by day the same pigment will migrate inwards and assume the position which distinguishes the light-adaptation. The same diurnal independent migration of the retinal (proximal) pigment was found by Bennit (1932) in *Cambarus* and by Welsh (1935) in *Penaeopsis goodei*. In 1935 the latter detected a diurnal migration of the reflecting pigment-cells in *Latreutes fucorum*, *Leander tenuicornis*, and *Leander affinis*, and in 1936 he observed the same phenomenon in both the distal pigment-cells and the reflecting pigment-cells in *Anchistioides antiguensis*.

The common occurrence of a diurnal rhythm in the movements of the eye-pigments in Crustacea shows with certainty that the influence of light on the pigment-cells is neither direct nor decisive. Later investigations by Bennit (1929, 1932) on *Cambarus* corrected the old opinion and proved that there really is a certain effect of the illumination of one eye on the position of the pigments in the other covered eye of the same animal in *Cambarus*, *Cancer*, *Carcinides* (*Carcinus*), *Libinia*, and *Homarus*. Thus either a nervous or a humoral regulation of the migrations of the eye-pigments must be supposed. Bennit hinted already in 1924 at the possibility of a hormonal control of these functions, but did not regard it as very important; later he (1932) and Parker (1932) discussed the same view more seriously. Since Welsh was able to prevent the diurnal rhythm under constant illumination by ligation of the eye-stalk, the humoral hypothesis has been more and more emphasized, and Welsh (1930) expresses his opinion in the following words: 'The normal movements of the distal pigment-cells as well as the periodic movements under constant external conditions appear to be controlled directly by the blood and indirectly by way of the nervous system.' Finally the theory of a hormonal regulation of the migration of the eye-pigments in Crustacea was definitely proved by Kleinholz (1934, 1936) in *Palaemonetes vulgaris*. The following results are taken from Kleinholz's paper.

Specimens of *Palaemonetes* (which species does not show any diurnal rhythm, either in the migrations of the integumentary,

or in the retinal pigments), which had been exposed to light so that their retinal pigments were in positions characteristic for light-adaptation, were injected with extracts of the eye-stalks of the same species. These were prepared in one series from animals that had been kept in darkness overnight, in another from animals kept on a black background. No significant change in the position of the distal pigment-cells was observed. On the other hand, eye-stalk extracts prepared from light-adapted animals and injected, in the dark, into *Palaemonetes* in which the retinal pigments had assumed the darkness position, brought about a proximal migration of the distal pigment-cells towards the position typically found in light-adapted animals (Fig. 18). At the same time, a histological study of the eyes of injected *Palaemonetes* proved that not only the distal pigment, but also the reflecting pigment, had migrated into the position characteristic for the light-adapted eye. The proximal pigment did not undergo any change in position. Eye-stalk extracts, prepared from animals adapted to darkness, when injected into dark-adapted *Palaemonetes* in darkness were also able to induce the migrations of the distal and reflecting pigments into the position typical for light-adapted animals, but proved to be only half as potent as extracts prepared from the eyes of light-adapted animals.

The action of the pigment-activating substance is not limited to the species: extracts of the eye-stalks of *Cancer irroratus*, *Libinia dubia*, *Uca pugilator*, and *Carcinides* (*Carcinus*) *maenas*, when injected into dark-adapted *Palaemonetes*, also affected the migrations of the distal and the reflecting pigments. Controls with extracts of other organs of *Palaemonetes* did not show any influence upon the retinal pigment migrations. It is, however, difficult to understand why extracts from the eye-stalks of *Callinectes sapidus*, in the concentrations used, did not affect the migration of the eye-pigments of *Palaemonetes*.

Kleinholz (1936) discusses the possibility of an identity between the chromatophorotropic hormone found in the eye-stalks of Decapods and the hormone inducing migration of the retinal pigments. Both have their sources in the eye-stalks, and 'dark-extracts' of *Palaemonetes* were found in both instances (cf. p. 114) to be only half as active as 'light-extracts'. Because Kleinholz did not find any conclusive response in the migration of the

eye-pigments in *Palaemonetes* to injection of extracts of *Callinectes* (which have a very strong influence upon the contraction of the chromatophores), he concludes that the Crustaceans may possess several hormones acting upon the integumentary and

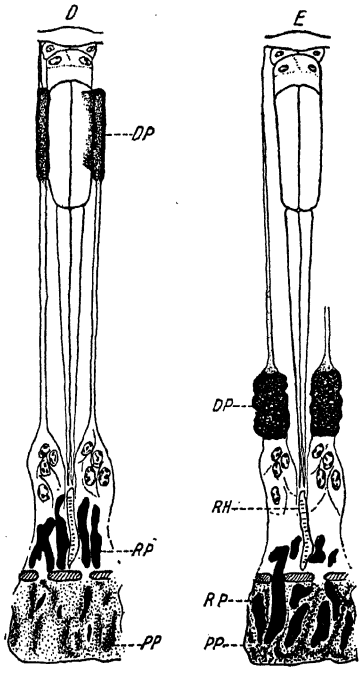


FIG. 18. Ommatidia from the eyes of *Palaemonetes vulgaris*, showing the general structure and the position of the three pigments under various conditions. *L*, from an eye in the light condition; *D*, from a dark-adapted eye; *E*, from an experimental animal which, after being adapted to darkness, was injected with stalk-extract prepared from the eyes of light-adapted specimens; *C*, cornea; *DP*, distal pigment; *PP*, proximal (retinal) pigment; *BM*, basement membrane; *RP*, reflecting pigment; *RH*, rhabdome. After Kleinholz.

the retinal pigments. Abramowitz (1937) also discusses this problem and writes:

'The key to the whole situation lies in the behaviour of the red and yellow chromatophores in animals (*Palaemonetes*) maintained in darkness. If Brown (1935) is correct in noting that the more usual condition of the red and yellow pigments of animals main-

tained in darkness was slight dispersion, and that a long sojourn in darkness resulted in the same condition of these pigments as that occurring when animals were adapted to a red background, there is little reason for postulating separate autocoids for the body and retinal pigments. Threshold differences would account for the various responses. If the earlier observations of Perkins (1928) that the red and yellow pigments are contracted in darkness is correct, the existence of separate hormones would be clearly indicated (because the chief body-pigments would react completely independently of the retinal pigments in darkness and on an illuminated black background), and the entire problem would be greatly simplified.'

Now my observations on the chromatophores of *Palaemonetes*, like those of Perkins (1928), show that the red and yellow body-pigments are completely concentrated in darkness, and the observation that a long sojourn in darkness results in an expansion of the same pigments may perhaps be explained by a complete absence of the pigment-concentrating hormone, since Abramowitz has shown that light seems to be necessary for its production (p. 113). Further, it is a fact that the red and yellow pigments are expanded in light on a black background but concentrated in light on a white background. In both instances, however, the distal and the reflecting retinal pigments assume the position characteristic for light-adaptation, and therefore it seems difficult to believe that the movements of the body-pigments and the eye-pigments are influenced by the same hormones (Hanström, 1937). In the vertebrates, too, it seems uncertain whether the melanophore hormone has any influence on the pigment migration within the retina (Jores, 1935, Matuo, 1935). In this connexion it may finally be added that the pigment-migration in the compound eye of some insects, for instance *Mantis religiosa*, has also been suspected of being regulated in a hormonal manner (Friza, 1928). The migration takes place in the iris pigment cells, is independent of direct stimulation by light, and adapts the eye for seeing in darkness through migration in a proximal direction (cf. Uchida, 1934, and Horstmann, 1935).

B. **Summary of Hormonal Functions, More or Less Certainly Connected with Incretory Eye-stalk Organs in Higher Crustaceans.** With a more or less high degree of probability, the following functions are supposed to be connected with the eye-stalks in higher Crustaceans.

The only hormonal function which—as it seems—can unquestionably be referred to a definite incretory organ in the eye-stalks is the pigment-activating hormone which has its source in the sinus gland (p. 119). Thus this gland produces the hormone (or the hormones) which contract the red and yellow chromatophores in *Palaemonetes vulgaris* (and other Decapods except the Brachyura), and expands the black and red chromatophores in *Uca pugilator* (and other crabs).

There exists some indirect evidence for the production of a substance within the eye-stalks which retards moulting, and since at the shedding of the cuticle certain substances are removed from the body, there may be an indirect connexion between an incretory organ in the eye-stalk and excretion. The uric acid is found, however, as solid pigment granules within the white chromatophores (p. 101). As far as we know at present, nothing prevents the supposition that the hormone which retards moulting is identical with the chromatophorotropic hormone and it would thus be derived from the sinus gland (p. 112).

A recent paper by Kalmus (1938) shows that the rhythmic motor activity in *Astacus* (increased at night) ceases after extirpation of the eyes, and that an injection of eye-stalk extracts after several days increases the activity again. Injection of water, Ringer solution, thiosulphate, and adrenaline did not bring forth this increase in muscular activity, whereas injection of eye-stalk extracts of *Crangon vulgaris* showed an evident positive effect. Thus it seems possible that the eye-stalks of Decapods produce a substance which regulates the rhythmic motor activity (at least in *Astacus*). A certain connexion between the motor activity and the chromatophoral functions is probably also found in *Hyperia* (p. 118).

A hormonal function which is certainly connected with some incretory organ in the eye-stalks of Decapods is the regulation of the migration of the retinal pigments (p. 127). As far as our present knowledge goes, this hormone is probably not identical with the chromatophorotropic hormone; nor is it proved that it is produced by the sinus gland, though it would not be surprising if this were so.

Kropp & Crozier (1934) and Navez & Kropp (1934) have found a growth-promoting effect of extracts of the eye-stalks of

Palaemonetes (p. 21) in plants, experiments which ought to be confirmed by further investigations. The active substance is cetainly not identical with the chromatophorotropic hormone (p. 107). There exists some rather indirect evidence for the supposition of a connexion between the chromatophoral functions (and thus also the chromatophorotropic hormone) and metabolism, especially fat-metabolism (p. 113). This possibility, as also most other problems recorded in this chapter, needs further extensive investigations, and is mentioned in order to show which problems are waiting to be solved in this field.

Although the incretory organs of the eye-stalks (the sinus gland and the X-organ; pp. 89 and 133) are the only anatomically well-known incretory organs of the Crustacea except for the more sporadically occurring medial frontal organ (p. 134) and the gonads (p. 35), and although all functions mentioned in the present chapter are ascribed to organs within the eye-stalks, one must be on one's guard against an over-estimation of the importance of the eye-stalks and their constituents for the normal functions of the crustacean body. The presence of the eye-stalks is not vital in all circumstances, for the Decapod Crustacea can be kept alive for months and years without eye-stalks (Megusar, 1912; Koller, 1930; Herbst, 1902). It has, however, not yet been shown whether the extirpation of the eye-stalks has any important influence upon sexual maturity, fertility, motor activity (cf., however, Kalmus, 1938), growth, and such things; and important incretory organs in vertebrates such as the adrenal medulla, the posterior pituitary, and in certain instances the thyroid gland have also been removed without serious results (Cameron, 1935). It seems possible that one incretory organ in the Crustacea may act as a substitute for another just as in vertebrates, and the anatomical investigation of the Crustacean body is far from complete.

XII

NEURO-SECRETORY ORGANS IN INVERTEBRATES

DURING the last twenty years several examples of neuro-secretory organs have been found in vertebrates; e.g. secretory nerve-cells in the medulla spinalis in fishes (Speidel, 1919, 1922) and in the diencephalon and mesencephalon in fishes, amphibians, reptiles, and mammals, including man (Scharrer, E., 1932–5). In connexion with the new concept of neuro-humoral action (Parker, 1932, 1936; Dale, 1935; Loewi, 1935) this is of special interest, since these structures represent a connexion between nervous and secretory tissues. During recent years in invertebrates too, several secretory organs have been detected that are intimately related to nervous structures or even constitute groups of nerve-cells, showing evident histological signs of a secretory activity. Such organs or portions of organs are described in Crustacea by Hanström (1931, 1934, 1937), in Insecta by Weyer (1935), Hanström (1936), and Scharrer, B. (1937), in Polychaeta by Scharrer, B. (1937), in Opisthobranchia by Scharrer, B. (1935) and Gaupp & Scharrer, E. (1935), and in Cephalopoda by Young (1936) and Thore

1. The X-organ and the Medial Frontal Organ in Crustacea

The X-organ has so far been found in the following groups of Crustacea: Leptostraca (Ståhl, 1938), Cumacea (Ståhl, 1938), Anaspidacea (Hanström, 1934), Mysidacea (Dohrn, 1906; Hanström, 1933, 1937), Euphausiacea (according to an unpublished paper by Carlson), Decapoda (Hanström, 1931, 1933, 1934, 1937; Boräng, 1933), and Stomatopoda (Hanström, 1931, 1934).

The X-organ is found in two rather different forms, one more compact, occurring in most species thus far investigated, and one hollow, sac-like, as yet detected only in the Mysidacea and the Cumacea.

Especially in higher stalk-eyed Crustaceans there is often

found a small sense organ in the form of an appendage of the eye-stalk with apically very thin cuticle, the eye-papilla (Plate XIII, 1), which is sometimes reduced and represented by a mere thinning of the cuticle: the sensory pore. When this eye-papilla or sensory pore is present it is always closely connected with the X-organ in position and innervation. Sometimes (in *Acanthephyra*) a branch of the eye-papilla nerve enters the X-organ on its way to the nervous centre in the medulla terminalis of the brain (which centre in most stalk-eyed Crustacea is situated in the eye-stalk; cf. Plate X). In all cases the nerve of the papilla is united with the nerve of the X-organ in the proximal portion of the path to the brain. In *Homarus americanus* (Plate XI, 1) the distal portion of the X-organ further contains small cells without secretory function which in their structure agree fairly well with the bipolar sense cells of the eye-papilla in several shrimps (*Parapasiphae sulcatifrons*). The proximal portion contains ordinary secretory cells. All these facts are in favour of the hypothesis that the X-organ represents the transformed sensory cells of a rudimentary eye-papilla which for the most part have moved inward and taken over a new secretory function (Hanström, 1937). The eye-papilla, which is found in the form of a papilla or sensory pore in higher Crustacea, represents probably in its turn the lateral frontal organ of lower Crustacea, a sense organ whose functions are unknown.

In lower Crustacea a medial frontal organ is also found which in the higher members of the group sometimes shows the same transformation of its structure as the lateral frontal organ. For in Decapoda, as in *Emerita analoga* and *Hippa talpoida*, and in Stomatopoda, as in *Squilla mantis*, there exist obvious signs of a secretory activity in the cells of the medial frontal organ. Thus both the lateral and the medial frontal organs in Crustacea represent the same transformation of a sensory organ into a secretory organ as is found in the pineal organ of vertebrates. In both instances the peripheral sensory apparatus is reduced, whereas the proximal portions of the rudimentary organs undergo a transformation of structure and function and show a progressive development and incretory activity.

Although the X-organ (and the medial frontal organ) are in

my opinion not true neuro-secretory structures, since they are derived from sensory organs and sensory cells and not from true nervous organs and ganglion cells, it seems natural to treat them under this heading. For the first X-organ described by me in *Squilla mantis* was situated completely within the brain and was surrounded on all sides by nerve-cells; and the structure of the nuclei was also roughly the same as in the common type of ganglion cells (Plate XI, 2).

The most thoroughly investigated X-organ occurs among the Decapods. It is found in almost all species thus far investigated. Only in *Cambarus*, *Astacus vulgaris*, *Sesarma cinereum*, *Aratus pisoni*, and probably in *Uca pugilator* can no traces of the X-organ be detected. In stalk-eyed Crustaceans and thus also in Decapods, the X-organ is normally situated in the eye-stalks, but in several Anomura with more or less rudimentary eyes (*Gebia affinis*, *Gebiopsis deltaura*, *Hippa talpoida*, *Emerita analoga*) its position is in the anterior part of the cephalothorax in close proximity to the brain.

In the Natantia (Plate X, and XII) the X-organ is shaped like a cluster of grapes, surrounding the nerve from the medulla terminalis. It is surrounded by the same sheath of connective tissue, the neurilemma, as also protects the central nervous system. This tissue forms a thin sheath with flat nuclei around each separate grape of the cluster. Each such portion of the organ contains several X-cells, whose nuclei are completely round and resemble the nuclei of the ganglion cells of the most common type in the Decapod brain. They have a large nucleolus and several chromatin granules.

The incretory function of the X-organ is shown cytologically by the presence in the protoplasm of different secretory products, and by the fact that it is ductless. The secretory products are in part small droplets of an eosinophil and fuchsinophil substance, in part larger irregularly shaped concretions of a concentric structure. The concentric structure seems, at least in some instances, to be due to the occurrence in the X-cells of fine, spirally coiled or concentrically arranged threads. Sometimes the secretory elements contain large empty vacuoles with a thin peripheral sheath of protoplasm and an excentrically situated nucleus (Plate XII). It is probable that all these structures in the X-cells only represent different stages in the

production of the same secretory substance, which in different phases or physiological circumstances reacts chemically in a different manner. It is possible that the small eosinophil droplets constitute the first stage of the development of the larger concentric concretions, which substances are either used up in the living animals or perhaps have been extracted during the fixation or other processes which precede the making of the histological preparations. The large, empty vacuoles can be best observed in preparations fixed in Bouin's fluid, whereas after fixation in Zenker's or Flemming's fluid they are mostly filled with a stained substance, certainly liquid in the living animals.

In the Decapoda Natantia the X-organ commonly reaches outwards as far as the hypodermis of the eye-stalk (Plate X), or as far as the proximal portion of the sense-cells of the eye-papilla or the sensory pore. In the Decapoda Anomura and Decapoda Brachyura the organ is situated in close proximity to the medulla terminalis, commonly far from the hypodermis. In most other orders of Crustacea, i.e. the Leptostraca, Anaspidacea, Euphausiacea, and Stomatopoda, it is in general of the same structure as in most Decapoda. In the Leptostraca (*Nebalia bipes*) the concentric concretions are unusually well developed, and in the Stomatopoda (*Squilla mantis*) the secretory droplets are very large and stain intensely (Plate XI, 2).

The X-organ in the Mysidacea (*Eucopia*, *Boreomysis arctica*) has an unusual form. It is sac-like and situated at the base of the eye-papilla (Plate XIII, 1). A common nerve from the medulla terminalis goes both to the papilla and to the X-organ. The X-organ in the Mysidacea was at first described by Dohrn (1906), who believed it to constitute the 'ganglion of the eye papilla'. Whereas the X-organ in most Crustaceans is made up of several clusters of cells, containing a number of small vacuoles, in *Eucopia* and *Boreomysis* it contains one large vesicle, surrounded by a single layer of cubical epithelial cells. The protoplasm of these cells in *Eucopia* possesses no sharp boundary against the granulated colloid in the vesicle, which thus seems to be directly connected with the protoplasm of the surrounding cells. Within the stained coagulum some clear vacuoles which do not stain are found. The large vesicle in *Boreomysis* is filled with intensely stained, winding threads instead of the granulated colloid found in *Eucopia*.

In the Cumacea Oelze (1931) described an organ which was supposed to be a statocyst. According to Ståhl (1938), however, this organ has in *Diastylis rhatkei* roughly the same structure as the X-organ in *Eucopia* since it is sac-like and filled with a granulated coagulum with clear spaces which do not stain. It seems more probable that this organ is really an X-organ, especially as it does not contain any statoliths.

2. Neuro-secretory Cells in the Brain of Various Invertebrates. The Stellate Ganglion and the Corpus Subpedunculatum in Cephalopods. Chromaffine Cells in the Ganglia of Annelida

In this section on 'Neuro-secretory organs in invertebrates', several different structures are included, because our present knowledge of neuro-secretion in invertebrates is still more unsatisfactory than of that in vertebrates. Some of the organs described here, i.e. the corpus epistellatum in Cephalopods and the X-organ, seem to have been originally nervous or sensory structures which became rudimentary but later acquired a new function. These (and in this connexion perhaps also the corpora cardiaca in insects (p. 54) should be mentioned) might be compared with the pineal organ and the nervous constituent of the hypophysis in vertebrates; they are true endocrine organs. The function of the corpus subpedunculatum is not known with certainty, but it is at least intimately connected with the nervous system, whereas the secretory cell-groups within the brain or other ganglia of different invertebrates and the chromaffine cells of the Annelida seem more truly to represent a neuro-secretory or neuro-humoral (Parker, 1932) activity. Between the cell-groups within the ganglia and the rest of the nervous tissue there is no sharp morphological boundary, and except for the traces of secretory activity which they show, these cells seem to possess a normal nervous structure with neurites and dendrites, and thus probably also function as true nerve-cells simultaneously with their secretory action.

By the name of corpus subpedunculatum, Thore (1936) described an organ occurring in the Cephalopoda which is situated beneath the pedunculus lobi optici of the brain. The organ is in part surrounded by the ganglion cells of the optic centres, contains small basophil cells and a number of blood-vessels, and

probably has a secretory function. This function is much more obvious in the corpus epistellatum in the Cephalopods, which, according to the investigation of Young (1936), represents one of the most beautiful instances of the transformation of a nervous into a secretory organ in invertebrates.

In Decapod Cephalopods there exists a system of giant nerve-fibres which probably serves to produce the rapid contractions

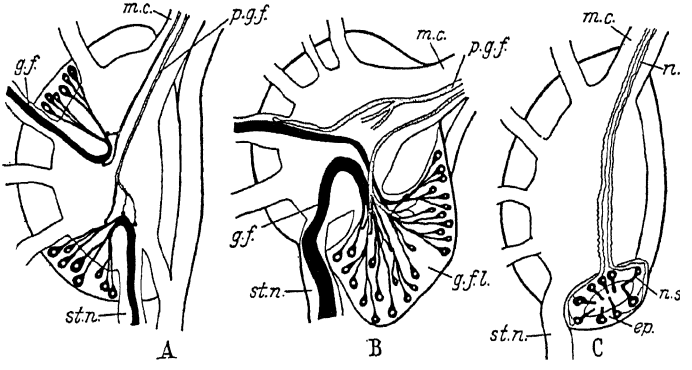


FIG. 19. Diagrams of stellate ganglia of Cephalopods. In *Sepia* (*A*) the giant fibres arise from cells scattered throughout the ganglion, and in *Loligo* (*B*) from cells collected into a giant fibre lobe. In Octopods (*C*) there are no giant fibres, but in the position of the giant fibre lobe are the cells whose axons end blindly in the epistellate body. *ep.* epistellate body; *g.f.* 'post-ganglionic' giant fibres; *g.f.l.* giant fibre lobe; *m.c.* mantle connective (pallial nerve); *n.* nerve to epistellate body; *n.s.* neurosecretory cells; *p.g.f.* 'pre-ganglionic' giant fibre; *st.n.* stellar nerve. After Young.

of the mantle muscles and the ink-sac by means of which the animals shoot backwards behind a cloud of ink. As Young has shown, these giant fibres in the stellate nerves do not arise from single giant cells in the ganglion stellatum, but in a very unusual way as syncytia by the fusion of the processes of a large number of small cells (Fig. 19). In *Sepia* these small cells are scattered throughout the ganglion, but in *Loligo forbesi* all cells giving rise to the giant fibres are connected together into a giant fibre lobe. The giant fibre lobe is situated in the hind portion of the stellate ganglion, where 300–1,500 cells fuse their processes to build up the giant fibres. In the Octopoda there are no giant fibres, but in the position of the giant fibre lobe there is a small closed vesicle, the epistellate body, which in

some species is pigmented yellow. Young suggests that the epistellate body has arisen from the giant fibre lobe, which has about the same position,

The epistellate body sometimes contains an optically homogeneous substance which stains readily with nigrosin and anilin blue, but not with basic dyes, or with any of the common acidic stains such as eosin, orange G, or acid fuchsin. The content of the vesicle shows considerable differences between individuals of a single species, differences which are perhaps correlated with some cycle of activity. In the walls of the vesicle there are curious cells, the neuro-secretory elements, whose general structure resembles that of nerve-cells, but whose inner processes, the axons, end blindly, embedded in the homogeneous substance within the cavity. The neuro-secretory cells are innervated by a small nerve which reaches them from the mantle connective.

After removal of both epistellate bodies in *Eledone moschata* the animals show general muscular weakness for some days and a lighter colour of the body. According to Young this is due to the lack of tone in the muscles, since the expansion of the chromatophores in Cephalopods is controlled by muscles (p. 79).

In connexion with the results obtained by Young it may be mentioned that Parker (1932) suggested that the giant nerve-fibres in the earthworm (Stough, 1926, 1930) and the Crustacea (Johnson, 1924, 1926) may exert their effects on the muscles by the liberation of some substance at the periphery. According to Young the same phenomenon may take place in the giant fibres of Decapod Cephalopods, whereas in the Octopods the fibres which no longer run to the muscles end blindly in the cavity of the corpus epistellatum, where they produce a substance which is carried away with the blood-stream to the muscles. In this connexion it may be added once more that Ungar & Zerling (1936) and Ungar (1937) have detected a substance in the blood of Cephalopods which acts upon the heart (p. 76) and the muscles of the stomach, and was obtained in the blood after stimulating the central ends of different nerves. It is possible, though still not definitely proved, that the nerves in this instance secrete into the blood a substance (tyramin?) which activates the heart.

Though it seems unquestionable that the brain of such Insecta

as the Lepidoptera acts as an incretory organ during metamorphosis (Kühn & Piepho, 1938), it is curious that Schrader (1938) was not able to detect any secretory cells within the brain of *Ephestia kühniella* (p. 64), especially as such neuro-secretory cells have been described by other authors in several insects.

The secretory cells described by Weyer (1935) in the brain of the Hymenoptera (*Apis mellifica*) are situated in the pars intercerebralis of the protocerebrum, and are with certainty real nerve-cells. These cells are, however, distinguished from the common ganglion cells of the brain by the occurrence of a number of secretory droplets which characterize them as neuro-secretory. The droplets stain intensely with common dyes used for staining nuclei, but less intensely with acidic dyes. In the brain of *Rhodnius prolixus* (Hemiptera, which species was investigated by Wigglesworth (pp. 60 and 66) for an incretory regulation of metamorphosis), I have detected some large cells which with a considerable degree of probability show signs of secretory activity (Plate XIII, 2). Their cytoplasm contains intensely staining eosinophil and fuchsinophil colloid-like droplets. It is especially interesting to notice that these cells are situated in the pars intercerebralis at the very place where, according to Pflugfelder (1937), those large cells are situated from which the nerve to the incretory corpora allata arises. In another member of the Hemiptera, *Lygaeus equestris*, there exists a certain very large lobus dorsomedialis within the pars intercerebralis which has not been found in other Hemiptera thus far investigated (Hanström, 1936). The lobus dorsomedialis is probably connected with the path of the median ocelli, and contains a probably syncytial nervous tissue with very large nuclei. These are irregularly shaped and contain a number of chromatin granules and curiously constructed nucleoli. The signs of a neuro-secretory activity in the lobus dorsomedialis of *Lygaeus* are, however, much less obvious than in the brains of *Apis*, *Rhodnius*, or of those insects whose neuro-secretory cells have been described by Scharrer, B. (1935, 1937).

In her first publication Scharrer (1935) gave a histological-cytological study of certain nerve-cells in the cerebral and other ganglia in the molluscs *Aplysia limacina* and *Pleurobranchaea meckeli* (Fig. 20), which according to the preparations show a very obvious secretory activity. The secretory substance is

found in the cytoplasm as small droplets or colloid-like masses in vacuoles which arise within the protoplasm as granules, stain intensely red or orange with van Gieson's stain, and are transported away from the cells by means of their nervous processes. Later, Scharrer (1936) published discoveries of similar cells in the brain of Annelida (*Nereis virens*) in which they are situated in the posterior portion of the brain in the neighbourhood of

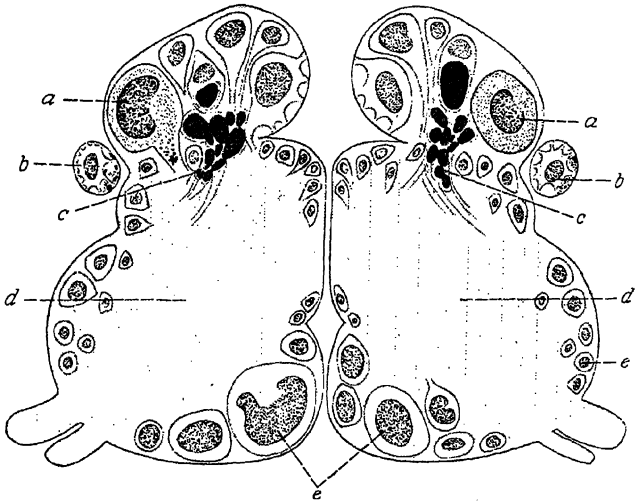


FIG. 20. Cerebral ganglia in *Pleurobranchaea meckeli*, schematic. *a*, *b*, *c* neurosecretory cells; *d* neuropil; *e* nerve-cells. After B. Scharrer.

the second pair of optic nerves, and (1937) in several other Annelida (*Nereis pelagica*, *Nereis diversicolor*, *Aphrodite aculeata*, *Lepidonotus squamatus*, *Lumbricus terrestris*, and *Hirudo medicinalis*), Mollusca (*Aplysia depilans*, *Tethys leporina*, *Doris tuberculata*, and *Aeolis papillosa*), and among the Insecta in *Bombus*. As Gaupp & Scharrer, E. (1935) point out, the same phenomenon is found in the brain of representatives of all classes of vertebrates, where colloid-like secretory products which stain intensely with van Gieson's stain are formed in cells which probably function simultaneously as nerve-cells. It is not necessary to emphasize that in all instances of so-called neurosecretory activity in the brains of invertebrates which have been demonstrated with purely cytological methods, physiological

experiments must decide whether the produced secretion has an incretory function or not.

Leydig (1857) already believed that certain ganglion cells with yellow granules in the central nervous system of Nematoda (*Mermis*), Hirudinea (*Pontobdella*), and Mollusca (*Paludina*) might be compared with the adrenal medulla. Later Poll &

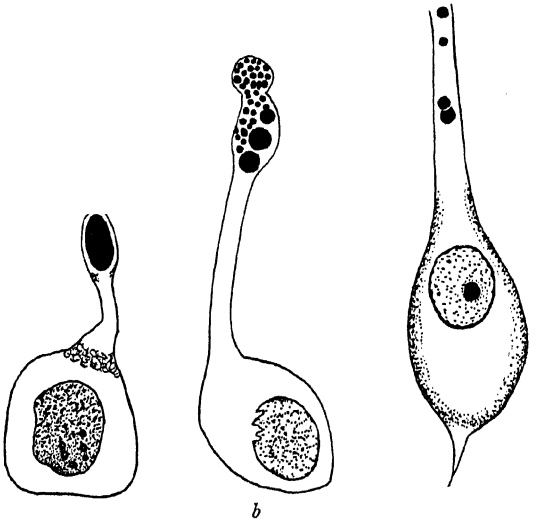


FIG. 21. Neuro-secretory cells with colloidal droplets (black). *a*, from cerebral ganglion of *Pleurobranchaea meckeli*; *b*, from nucleus praeopticus of the bony fish *Tinca vulgaris*; *c*, from nucleus paraventricularis of *Homo*. Simplified after Gaupp & Scharrer, E.

Sommer (1903), Poll (1909), Biedl (1912), Gaskell (1914, 1920), and Vialli (1934) (cf. also Ito, 1936) have discovered in the ganglia of several Annelida (*Aphrodite aculeata*, *Eunice gigantea*, *Lumbricus herculeus*, *Aulastomum gulo*, and *Placobdella catenigera*) chromaffine cells which according to Biedl and Gaskell really produce adrenaline or at least a substance very closely related to it. In *Hirudo medicinalis* these chromaffine cells occur in regular distribution in the ventral ganglia, four smaller cells in the lateral portions, two larger in the medial portion, and sometimes, in addition, a small seventh cell. Though the brown colour characteristic of the action of chromic acid on the chromaffine cells is not so specific as was earlier supposed, the

reaction is not without importance in this instance, since Biedl (1912) and Gaskell (1920) were able to extract from the ganglia of Hirudinea a substance which showed the same action on several organs as adrenaline, this latter substance being simultaneously administered for comparison. According to Biedl the active substance extracted from the worms may even be identical with adrenaline. Von der Wense (1938) has confirmed these observations, and with the method used for purifying adrenaline from the adrenal gland in vertebrates he has extracted a substance from *Hirudo* which has the same influence upon the isolated alimentary canal of the rabbit and on the isolated frog-heart as adrenaline.

According to the investigations just recorded the chromaffine cells in the Annelida constitute true ganglion cells with axons and neurofibrils. Although his opinion must be histologically confirmed, Gaskell (1920) even believes that the contractile muscular elements of the blood vessels are innervated by nerve fibres derived from the chromaffine cells, and that the sympathetic nervous system and the adrenaline-producing cells thus constitute a unity in Annelids, contrary to the condition in vertebrates. The anatomy and physiology of the nervous system in the Annelida have not been investigated so satisfactorily as to permit any certain conclusions regarding the correctness of this hypothesis, but it is of interest in this connexion that adrenaline in vertebrates is produced by the medulla of the adrenal gland which arises from embryonic sympathetic ganglia, and that a substance which is identical with or at least closely related to adrenaline is liberated at the nerve endings during the action of the sympathetic nerve-fibres in vertebrates (Dale, 1935; Loewi, 1935). It is further proved (pp. 13–18) that almost all invertebrates thus far investigated have given a positive response to adrenaline, and that this hormone or substances very closely related to it have been detected in several invertebrates (Protozoa, Annelida, Mollusca, Insecta; pp. 22–3). With a rather high degree of certainty it seems legitimate to regard adrenaline (or closely related substances) as the first detected hormone which has been proved to be universally active and probably universally present throughout the whole animal kingdom.

APPENDIX

ENDOCRINE ORGANS AND HORMONAL REACTIONS IN THE TUNICATA

WHEREAS most invertebrate groups are systematically so remotely related to the vertebrates that all comparisons must be mere analogies, the Tunicata together with the Acephala (*Amphioxus* and its relatives) and the Vertebrata constitute the Chordata. Thus it is possible to make comparisons between the Tunicata and the Vertebrata with a greater degree of certainty, and as an appendix the incretory organs and hormonal reactions of the Tunicata will be described here in just a few words.

The Tunicata not only possess an organ homologous with the thyroid gland in the endostyle of the respiratory portion of the digestive canal, but also an organ homologous (at least in part) with the pituitary in the subneural gland. The simplest form of this gland is found according to Huus (1937) in such Tunicata as *Distaplia*, where it is represented exclusively by the hindmost portion of the ciliated canal from the 'olfactory pit' which is lined with secretory cells. Through evagination and growth a morphologically more exactly defined organ is later developed which has a more complicated structure, and in the solitary Ascidians contains a system of branched canals. The secretory substance is probably produced by disintegration of the glandular cells within the walls of the canals. Julin (1881) and van Beneden (1884) already regarded the ciliated canal, the pit which opens into the pharynx, and the subneural gland as the homologues of the pituitary of vertebrates. According to Stendell (1914), however, only the subneural gland corresponds to the pituitary, and Huus (1937) holds the view that it can only be compared with the posterior lobe of the hypophysis, since it arises from the primary nerve-tube of the larva (cf., however, the paper of Hogg, 1937).

With reference to the action of vertebrate hormones on the Tunicata, Weiss (1928, 1930) fed the larvae of *Ciona intestinalis* with thyroid and found an acceleration of the metamorphosis, whereas pituitrin retarded it. Torrey (1928), on the other hand, observed a slower rate of cleavage and development in eggs of *Phallusia nigra* after treatment with thyroid extracts, and Ashbel (1925) noted an increased oxygen consumption in the ovaries of Tunicates under the influence of thyroxine.

Hykès (1926, 1932) investigated the action of various vertebrate hormones upon the heart in Tunicates (species of *Salpa*). The

heart of the Tunicata is distinguished by its special manner of action. First the blood-stream is sent in one direction, and, after a pause, in the contrary direction. Hykès found that thyroid extracts stimulate the heart-beats in *Salpa*, especially the backwards directed pulsations. Adrenaline acted in the same manner, but simultaneously slowed down the pulsations directed forwards. Hypophysin 'Hoechst' and thymus extracts made the contractions slower, in which process, however, the hypophysin increased the strength of each single contraction, and the thymus extracts occasioned irregular contractions. Bacq (1934, 1935), however, was not able to notice any influence of adrenaline on the heart-contractions in another species, *Ciona intestinalis*; nor did he observe any action of acetylcholine upon the heart of the same species.

Our present knowledge of hormone production in the subneural gland of the Tunicata makes it probable that this gland can to a certain extent be compared physiologically with the pituitary in vertebrates. Butcher (1929, 1930) at first denied its function as an excretory organ, a slime or a salivary gland, and detected the oxytocic hormone in the subneural gland of *Molgula manhattensis*. Later Bacq & Florkin (1935) found in extracts of the same gland in *Ciona intestinalis* substances which possess the three typical actions of the posterior pituitary in vertebrates; they raised the blood-pressure in the cat, they stimulated the contraction of the surviving uterus in the rat and guinea-pig, and they expanded the melanophores in the skin of the frog.

In spite of Huus's opinion, that the subneural gland ought to be compared only with the posterior pituitary of vertebrates, Hogg (1937) seems to have found in the subneural gland of *Polycarpa tecta* the gonadotropic principle of the anterior pituitary, since extracts of this gland promoted the growth and development of the ovaries in immature mice. The number of test animals was, however, small, and the investigation ought to be repeated. Finally, Abramowitz (1937) tested extracts of the subneural gland in *Molgula manhattensis* upon invertebrates, injecting them into blinded specimens of the crab *Uca*. After extirpation of the eye-stalks in *Uca* the animals grow pale, since the chromatophores are completely contracted (p. 104). The chromatophores can again be caused to expand by injection of extracts of the eye-stalks of *Uca* or by intermedin from the vertebrate pituitary. According to Abramowitz the chromatophores in blinded *Uca* could also be caused to expand after injection of extracts of the subneural gland in *Molgula*, which latter, in agreement with the experiments of Bacq & Florkin (1935), must thus contain the same pigment-expanding principle (intermedin) as the hypophysis in vertebrates.

Finally, Huus (1937) sums up his opinion regarding the biological function of the subneural gland of the Tunicata in the following manner. The ciliated pit absorbs stimulating substances from the surrounding medium and transports them to the subneural gland, causing this organ to start its secretory activity. Although the ciliated pit is often called the 'olfactory pit' it is not innervated and thus has no connexion with the central nervous system. The incretory substance is then secreted into the blood and transported to the gonads, which are made to discharge the generative products. The simultaneous discharge of the sperm and the ova into the surrounding medium is of special importance to the attached and immobile Tunicata, which do not copulate and often live in deep water.

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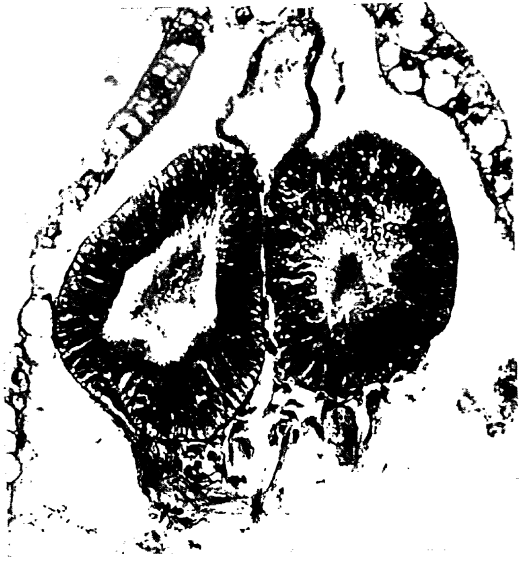
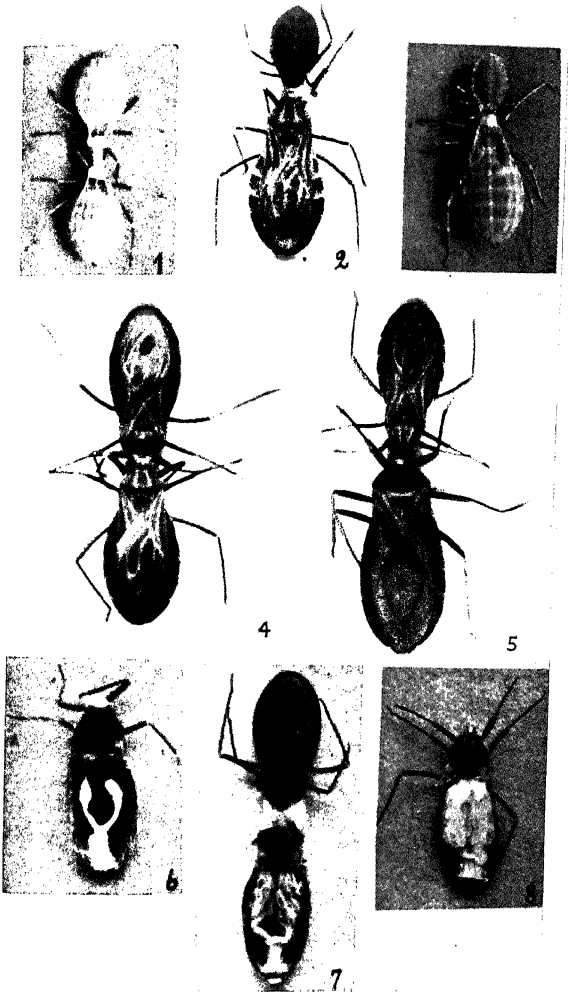


1. Horizontal section of the corpora allata in *Dixippus morosus*. Above and laterally, portions of the fat-body. Original.

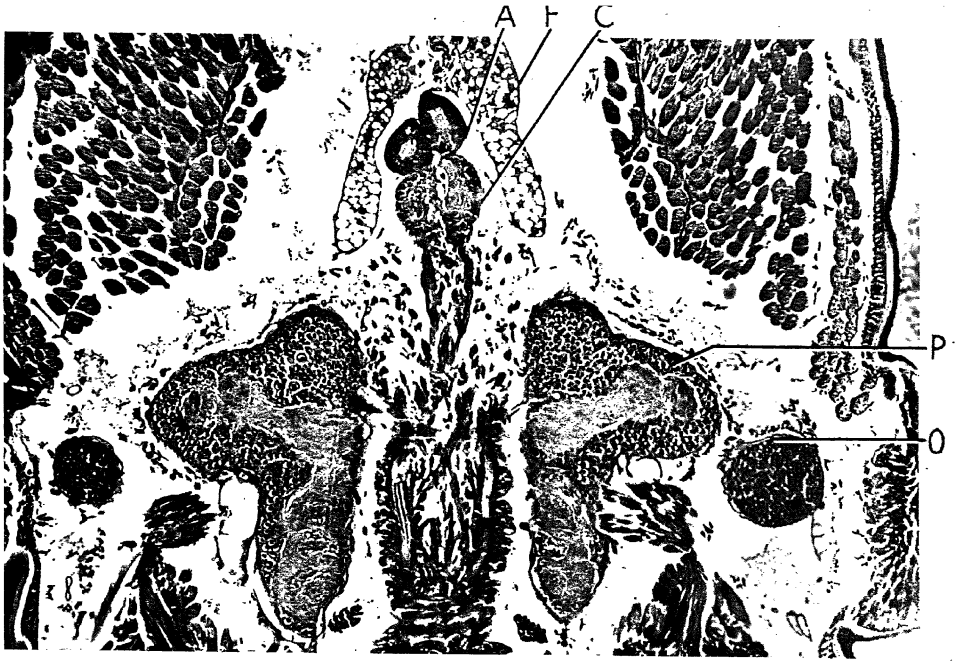
2. Horizontal section of the corpora cardiaca in *Dixippus morosus*. Above and laterally, portions of the fat-body; below and laterally, portions of the brain. Original.

PLATE I

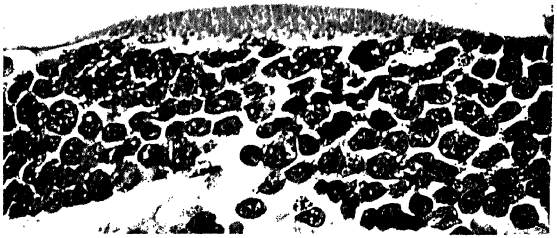


1. Two decapitated 4th-stage nymphs of *Rhodnius prolixus* connected by a capillary tube.
2. Adult female of *Rhodnius* with corpus allatum joined to decapitated 3rd-stage nymph.
3. Fifth-stage nymph *Rhodnius* (below) joined to third-stage nymph of *Triatoma infestans*.
4. Female *Rhodnius* with corpus allatum joined to female without.
5. Female *Triatoma infestans* with corpus allatum joined to female *Rhodnius* without.
6. Female *Rhodnius* 1 month after decapitation: no development of eggs in ovaries
7. Female *Rhodnius* showing egg-development in ovaries induced by joining to male *Rhodnius* with brain removed but corpus allatum intact.
8. Female *Rhodnius* 1 month after removal of the brain; the corpus allatum left intact.

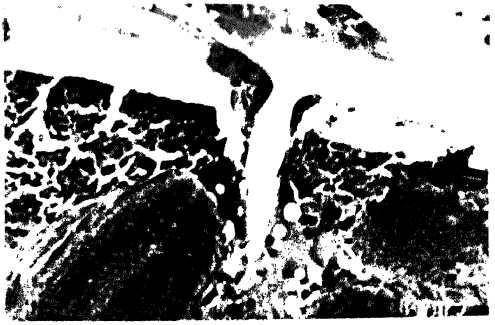
All figures after Wigglesworth (1936).



Horizontal section through the head of *Dixippus morosus*. Above: laterally, muscles of the head, medially, portions of the fat-body (*F*), the corpora allata (*A*), and the corpora cardiaca (*C*) (cp. plate I). Below: laterally, portions of the brain (protocerebrum (*P*), with the optic centres (*O*) and tritocerebrum); medially, muscles of the oesophagus. Original.



1.

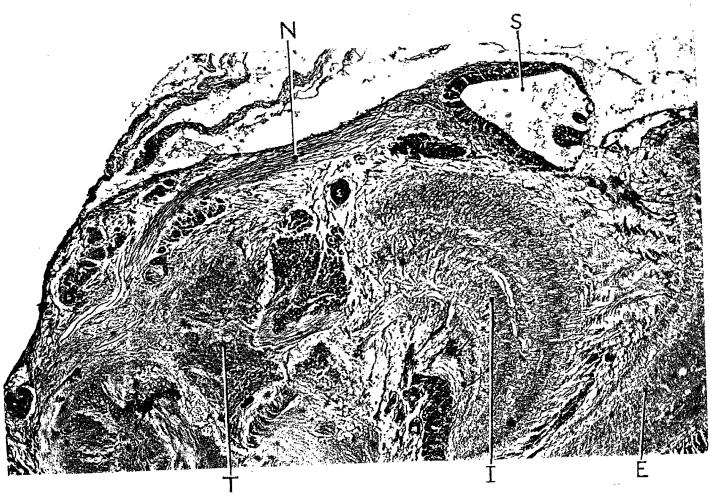


2.

1. Cross-section of the sinus gland in *Eucopia*. Beneath the gland, ganglion cells; above it, a blood sinus. After Hanström.
2. The cup-shaped sinus gland of *Palaemonetes vulgaris*. Below: the medulla externa and medulla interna of the optic centres; above: the outer blood sinus of the eye-stalk. After Hanström.
3. Cross-section through the inverse sinus gland of *Acanthephyra*. After Hanström.

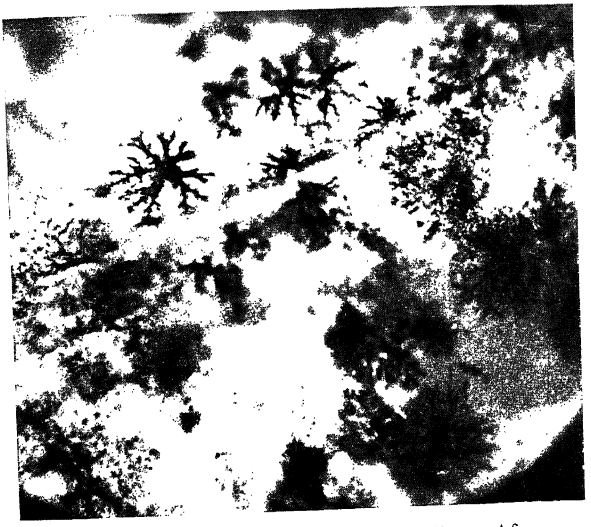
1. Sinus gland of *Homarus americanus*; to the left its nerve. After Hanström.

2. Everse sinus gland of *Hippa talpoida*. Above and to the left, a blood sinus, below, a portion of the brain (the protocerebrum). After Hanström.



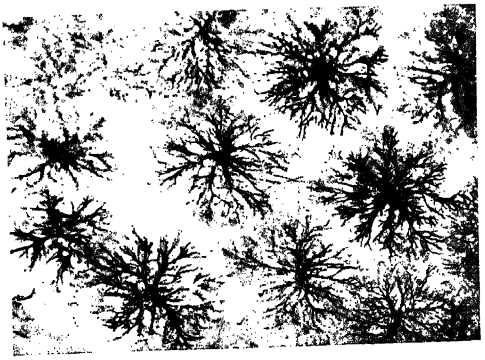
Longitudinal section of the lobus opticus in *Callinectes sapidus*. At the top: to the right the sinus gland (*S*), to the left its nerve (*N*). Below: from right to left a portion of the medulla externa (*E*), the medulla interna (*I*) (like a crescent), and medulla terminalis (*T*). After Hanström.

PLATE VI

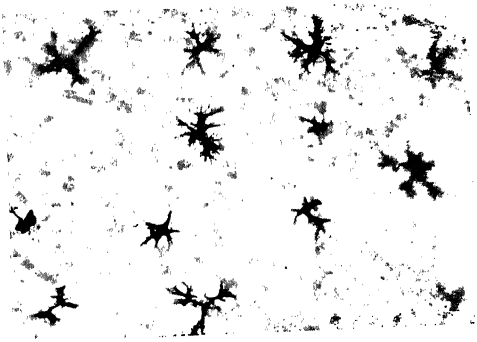


1. Expanded melanophores in *Uca pugilator*. After Sven Carlson.

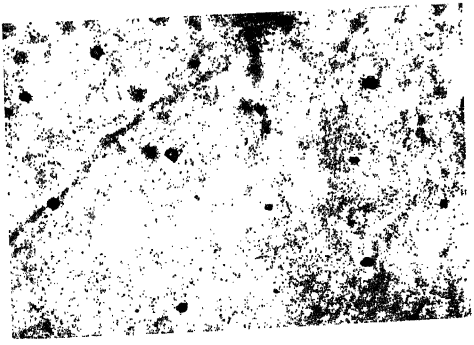
2. Contracted melanophores after eye-extirpation in *Uca pugilator*. After Sven Carlson.



1.



2.

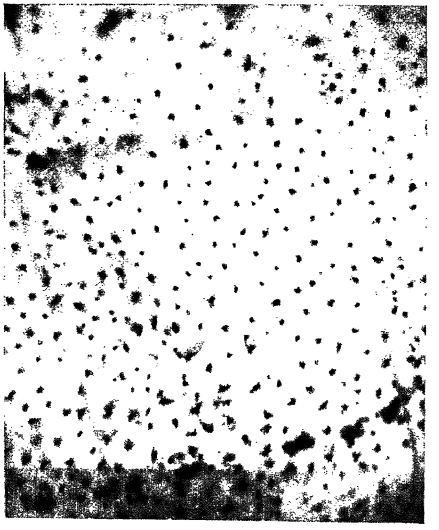


3.

1. Expanded red chromatophores from the telson of *Nephrops norvegicus* after eye-extirpation.
2. Chromatophores from the telson of the same animal (*Nephrops norvegicus*), as in fig. 1, 15 minutes after injection of an extract of the eye-stalks of the same species.
3. Chromatophores from the telson of the same animal 45 minutes after injection of the same extract, as in fig. 2.

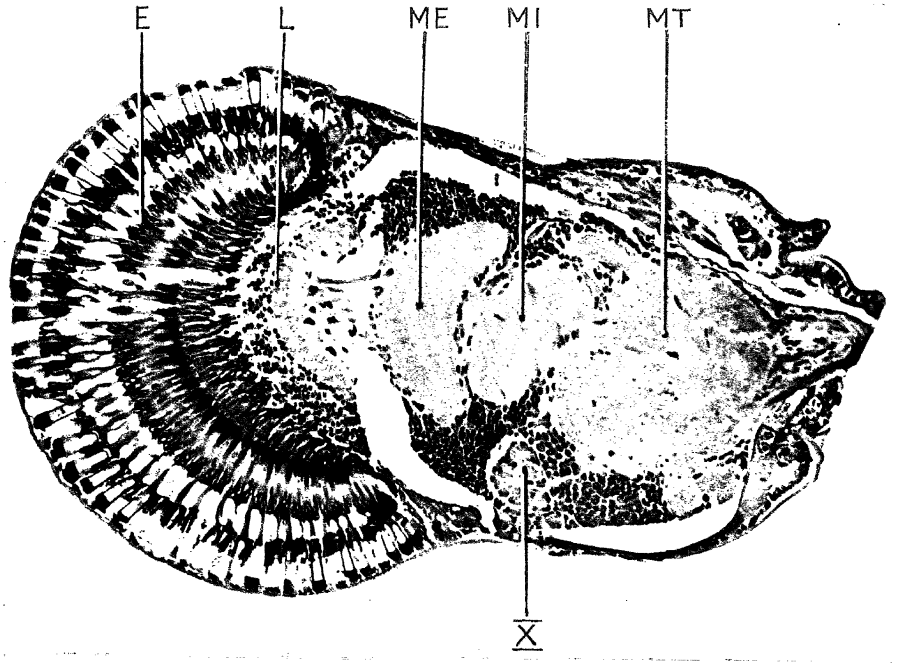
The chromatophores are photographed through a 'window' in the cuticle (cp. p. 104). After Sven Carlson.

1. Chromatophores from the dorsal portion of the abdomen in a blinded specimen of *Palaemonetes vulgaris*, 15 minutes after an injection of an extract from the distal third of the eye-stalks of *Pagurus pollicaris*. No action of the injection can be observed. After Hanström.



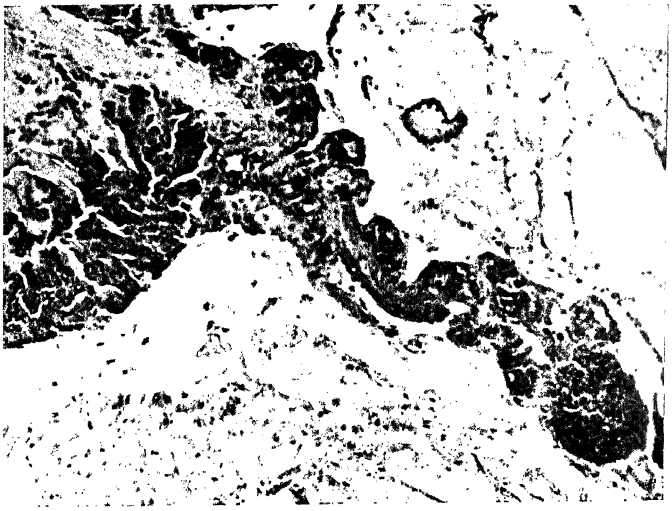
2. Chromatophores from the same region as in figure 1, 15 minutes after injection of an extract from the middle third of the eye-stalks of *Pagurus pollicaris*. The chromatophores are strongly concentrated. After Hanström.

PLATE IX



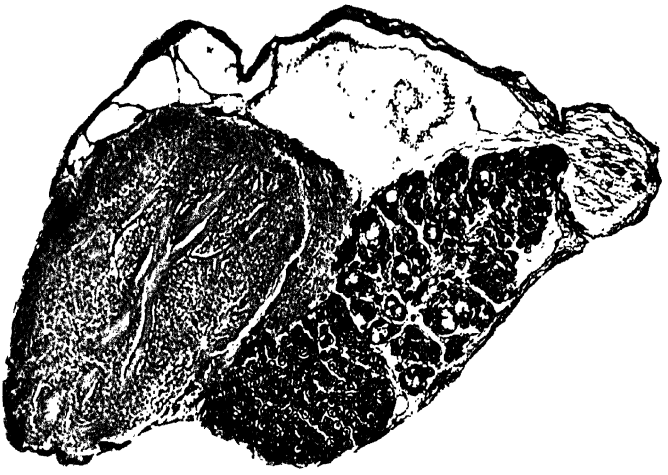
Longitudinal section through the eye-stalk in *Palaemonetes vulgaris*. From left to right: 1. the eye proper (*E*), and within its concavity the lamina ganglionaris (*L*), 2. the crescent-shaped medulla externa (*ME*), and medulla interna (*MI*), and finally 3. the medulla terminalis (*MT*). Beneath the medulla interna the X-organ (*X*). After Hanström.

PLATE X

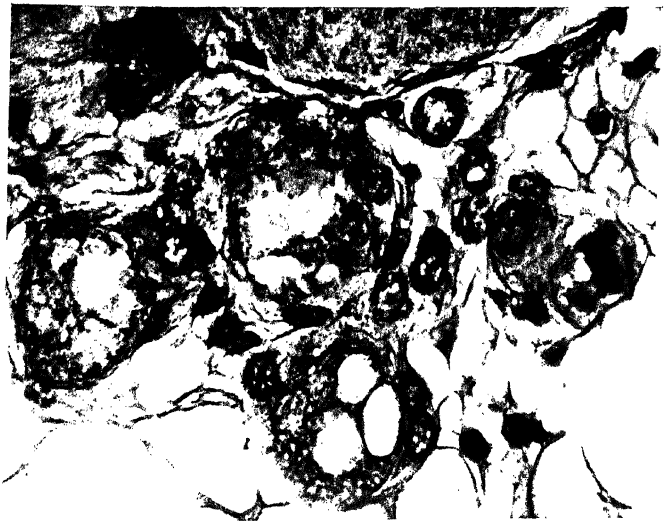


1. The elongated X-organ in *Homarus americanus*. On the left, the medulla terminalis. After Hanström.

2. The concentrated X-organ in *Squilla mantis* which is completely surrounded by ganglion cells. The black points of varying size are the secretory droplets, the grey spots are the nuclei. The droplets are most densely concentrated in the left half of the figure. Below and to the left a blood vessel. After Hanström.

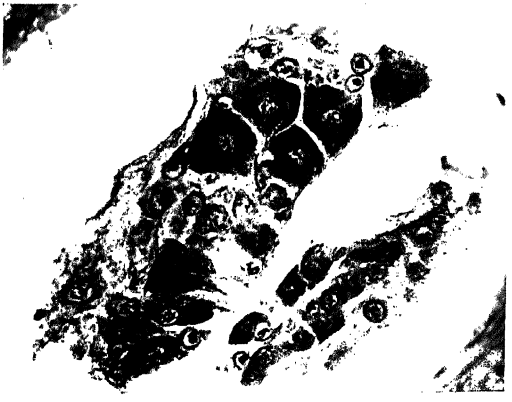


1. X-organ in *Acanthephyra*. To the left, a portion of the medulla terminalis; to the right, cross-section of the nerve of the eye-papilla, and between them the X-organ. After Hanström.



2. Portion of the X-organ in *Acanthephyra* in higher magnification. The cells contain vacuoles and secretory droplets. After Hanström.

1. Longitudinal section through the eye-papilla and the X-organ in *Eucopia*. The X-organ is sac-shaped and contains a coagulum. After Hanström.



2. Horizontal section through the dorsal portion of the protocerebrum of the brain in *Rhodnius prolixus*. Between the nuclei of the common ganglion cells some large polygonal, intensely staining, probably secretory nerve cells can be observed.